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Position Document 3

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CHLOROBENZILATE: POSITION DOCUMENT 3

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J.B. BOYD
PROJECT MANAGER
SPECIAL PESTICIDE REVIEW DIVISION
OFFICE OF PESTICIDE PROGRAMS
U.S. ENVIRONMENTAL PROTECTION AGENCY

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INFORMATION SERVICE
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CHLOROBENZILATE

Working Group

J. Boyd, Project Manager, OPP
D. Patton, Attorney, OGC
D. Barnes, Chemist, OTS
D. Kuroda, Physical Scientist, ORD
D. Dalton, Entomologist, PTSED

Technical Support Team

J. Boyd, Project Manager, OPP
M. Luttner, Economist, CED, OPP
D. Severn, Chemist, CED, OPP
R. Potrepka, Pharmacologist, CED, OPP
M. McWhorter, Entomologist, CED, OPP
D. Coppage, Aquatic Biologist, CED, OPP
D. Patton, Attorney, OGC
K. Keaney, Economist, OPP
E. Siegler, Attorney, OGC
D. Reed, Chemist, RD, OPP
G. Omara, Economist, CED, OPP
F. Kutz, Chemist, TSD, OPP
T. Dixon, Chemist, TSD, OPP

Pesticide Chemical Review Committee (PCRC)

W. Wells, Chairman, SPRD, OPP
D. Kuroda, Physical Scientist, ORD
J. Moore, CAG Liason, SPRD, OPP
A. Jennings, OPM
E. Anderson, CAG
M. Menotti, OGC
J. Neylan, PTSED

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I. Introduction

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the related regulations require the Environmental Protection Agency to review the risks and benefits of the uses of registered pesticides. On May 26, 1976, the Agency initiated this review for chlorobenzilate with the issuance of a notice of rebuttable presumption against registration and continued registration (RPAR) of pesticide products containing chlorobenzilate (41 FR 21517, May 26, 1976). Based on information developed through the RPAR review, this position document presents the Agency's analyses of the risks and benefits of chlorobenzilate uses and recommendations regarding regulatory alternatives.

A. Background[1]

1. Chemical and Physical Properties

Chlorobenzilate (ethyl 4,4'-dichlorobenzilate) is a chlorinated hydrocarbon which is also known by its trade names: Acarban, Akar 338, Rospin, Geigy 338, Benzilan, Folbex, and Kop-Mite. In pure form it is a yellowish-brown viscous liquid with a melting point of 35° to 37°C at 0.06 mm Hg and a vapor pressure of 2.2×10^{-6} mm at 20°C. It is highly soluble in most organic solvents and petroleum oils but is insoluble in water. The molecular weight is 325.2 and its structural formula is:

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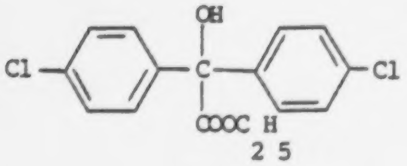
[1] The chlorobenzilate RPAR was one of the first RPARs issued by the Agency. At the time it was issued, Agency RPAR procedures were still in a formative stage, and a detailed position document did not accompany the chlorobenzilate RPAR. For this reason, the Agency has included in this position document information which under current procedures would appear in Position Document 1 and accompany the RPAR.



2. Registered Uses

Chlorobenzilate, an acaricide, is registered for use on almonds, apples, melons, cherries, citrus fruit, cotton, pears, walnuts, ornamentals, trees, and in certain outdoor areas. It is also registered to control spiders on boats and docks. Ninety percent of the current usage applied is on citrus crops (Table 1). There are 18 Federally-registered chlorobenzilate products; six applications for Federal registration are pending, and there are eight State-registered products for which notices of application for Federal registration were filed, pursuant to 40 CFR 162.17. All pending applications are for cites already registered.

3. Environmental Fate

Little is known about the metabolism of chlorobenzilate in man or other organisms or about its degradation in soil and water or by light. The primary reactions which chlorobenzilate is likely to undergo after field application may include hydrolysis, decarboxylation, conjugation, and oxidation. Chlorobenzilate soil persistence studies found that its half-life was 1.5 to 5 weeks, however, the degradation products were not identified or measured (Boyd, H., 1978).

Several studies show that chlorobenzilate is not metabolized by plants. In studies on apples (Murphy et al. 1966) and citrus fruit

Table 1

Agricultural Use of Chlorobenzilate, 1975[a]

Registered Uses	Site	Active Ingredients Used (Pounds)	All Agricultural Uses (%)[b]	Farms[c]		Acreage[c]	
				No.	%	No.	%
Citrus: Oranges, Lemons, Grapefruit	Fl	805,000	72.1	8,314	80.1	523,000	67.3
	TX	101,500	9.1	2,584	50.8	43,000	56.6
	CA	7,500	0.7	315	4.1	4,000	1.6
	AZ	6,000	0.5	207	6.7	3,000	2.8
	US	920,000	82.4	11,421	43.4	573,000	47.0
Other (Limes, Tangerines, elos, etc.)	US	75,700	6.8	N, A	-	47,000	45.9
All Citrus	US	995,700	89.2	11,421+	-	620,000+	50.9
Cotton	US	39,000	3.5	-	-	39,000	0.41
Fruits, Nuts, & Miscellaneous Crops	US	81,000	7.3	-	-	24,000	1
All Uses	US	1,116,000	100.0	-	-	715,000	-

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[a] Source: Preliminary Benefit Analysis (Luttner, 1977).

[b] Percent of total U.S. chlorobenzilate used on commodity noted.

[c] Percent is of total farms and total acreage producing each commodity.

(Gunther et al. 1955), chlorobenzilate was found only in the peel. Hassan and Knowles (1969) found that chlorobenzilate rapidly penetrated soybean leaves and was translocated unchanged into the leaf stalks.

Miyazaki et al. (1970) found that chlorobenzilate was metabolized to dichlorobenzophenone (DBP) by micro-organisms, especially yeasts. Horn et al. (1955) found that chlorobenzilate was hydrolyzed to the free acid (DBA) by dogs. Knowles and Ahmad (1971) found that chlorobenzilate is metabolized by rat hepatic enzymes to at least four and perhaps as many as seven metabolites. These results indicate that chlorobenzilate can be metabolized by microorganisms and animals. Figure 1 illustrates these routes and products.

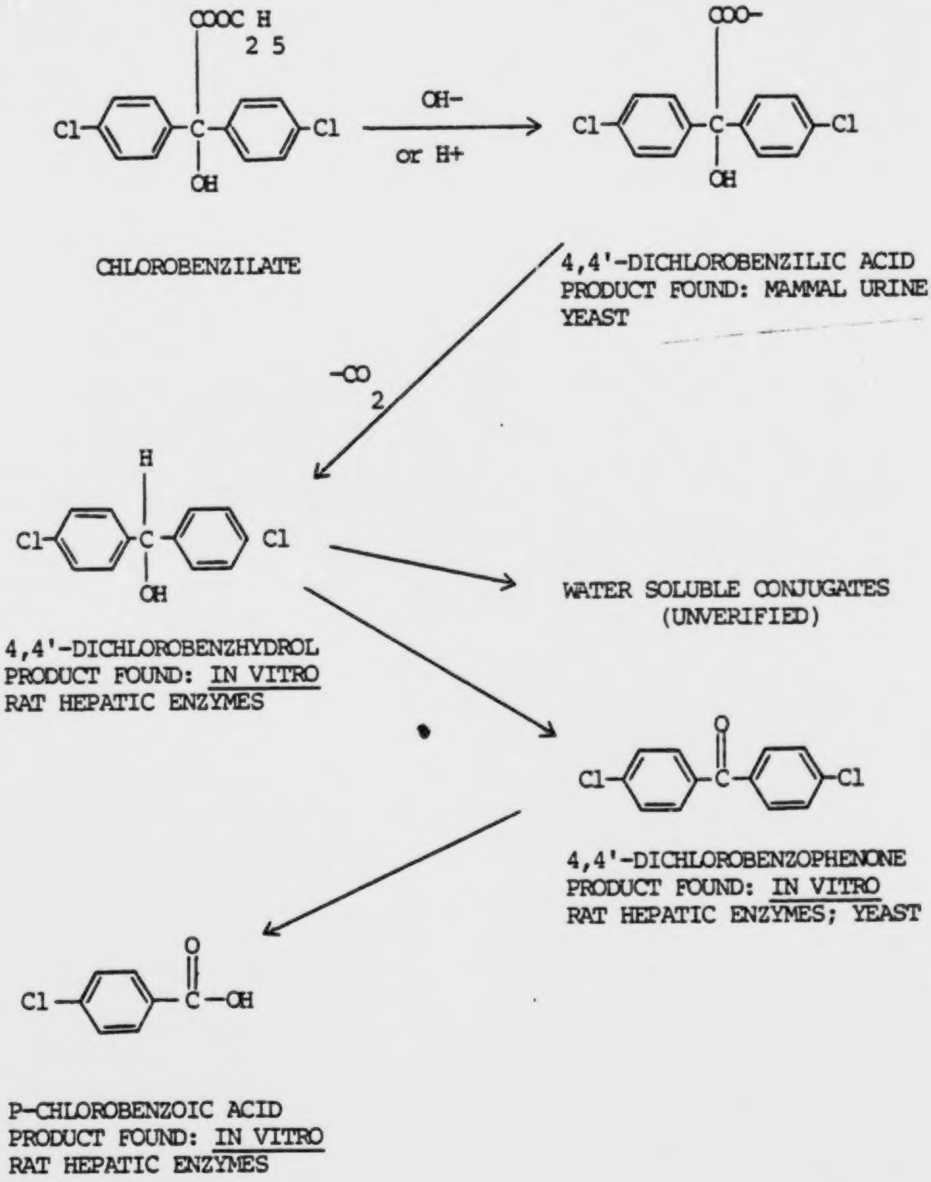
B. Regulatory History

Based on a study by Innes et al. (1969), an Advisory Committee to the Secretary of Health, Education and Welfare (the Mrak Commission), recommended that human exposure to chlorobenzilate be minimized and that use of this pesticide be restricted to those purposes for which there are benefits to human health which outweigh the potential hazard of carcinogenicity (DHEW, 1969).

On May 26, 1976 [pursuant to 40 CFR 162.11(a)(3)] the Agency issued a notice of rebuttable presumption against registration (RPAR) of pesticide products containing chlorobenzilate (41 FR 21517, May 26, 1976) based on studies in which tumors developed in rats (Horn et al. 1955; Woodard, 1966) and mice (Innes et al. 1969) which had been orally exposed to the pesticide. After the notice of rebuttable presumption was issued, the National Cancer

FIGURE 1

METABOLIC ROUTES OF CHLOROBENZILATE



CHLOROBENZILATE

4,4'-DICHLOROBENZILIC ACID
PRODUCT FOUND: MAMMAL URINE;
YEAST

4,4'-DICHLOROBENZHYDROL
PRODUCT FOUND: IN VITRO
RAT HEPATIC ENZYMES

WATER SOLUBLE CONJUGATES
(UNVERIFIED)

4,4'-DICHLOROBENZOPHENONE
PRODUCT FOUND: IN VITRO
RAT HEPATIC ENZYMES; YEAST

P-CHLOROBENZOIC ACID
PRODUCT FOUND: IN VITRO
RAT HEPATIC ENZYMES

Institute (NCI) completed a chlorobenzilate carcinogenesis bioassay which showed a statistically significant increase of tumors in mice. The Agency provided copies of this study to registrants who requested it; these data and EPA analyses of the data are summarized in Appendix A. Other toxicity data are summarized in Appendix B.

Registrants and other interested parties were offered an opportunity to review the data upon which the presumption was based and to submit information to rebut the presumption. Respondents could rebut the presumption by showing that the Agency's initial determination of risk was in error, or by showing that consideration of use patterns and exposure indicates that use of the pesticide is not likely to result in any significant chronic adverse effects [40 CFR 162.11(a)(4)]. Also, registrants and other interested persons were offered the opportunity to submit evidence as to whether the economic, social, and environmental benefits or the use of the pesticide outweigh the risk of its use [162.11(a)(5))iii)]. Although the presumption was based on three studies, the preliminary results of the NCI carcinogenesis bioassay were available, and comments were received on all four studies. The Agency received 35 submissions, 12 from chlorobenzilate registrants and 23 from other interested parties.

As summarized in Section II of this position document, the Agency has concluded that information submitted in rebuttal to the Horn and Woodard studies raises serious questions about the reliability of these data for assessing the oncongenicity of chlorobenzilate, and that the respondents have therefore successfully rebutted these data. The Agency has also concluded that respondents failed to rebut data in the Innes study and the NCI study. As a result, the Agency has used the Innes and NCI data to assess the risks associated with the uses of chlorobenzilate. In Section III, the Agency has analyzed information on the benefits of chlorobenzilate uses and the probable costs of regulatory action to cancel or otherwise restrict uses of this pesticide. An analysis of the risks and the social, economic, and environmental benefits which would result from each of six different regulatory options is presented in Section IV. Finally, Section V presents the Agency's recommended option and an explanation of why this option achieves a sound balance between the risks and benefits of the uses of chlorobenzilate considered in this analysis.

II. Analysis and Assessment of Risk

A. Analysis of Rebuttal Submissions[2]

Persons submitting rebuttals contended that data in the four studies were defective in several critical respects and that exposure to chlorobenzilate would not lead to significant adverse effects. The Agency has reviewed the carcinogenicity data again in light of the rebuttal comments, and has concluded that information and arguments submitted in rebuttal to the Horn and Woodard studies indicate that these data may not be reliable for assessing chlorobenzilate's oncogenic effects. Accordingly, the Agency accepts the rebuttal arguments against use of these data for assessing the cancer risk of chlorobenzilate. The Agency also has concluded that arguments and data submitted regarding the Innes and NCI studies did not rebut or otherwise invalidate the presumption that chlorobenzilate is oncogenic.

1. Successful Rebuttal Arguments

a. Horn et al. (1955)

Horn et al. administered chlorobenzilate in the diet to rats from weaning until 104 weeks of age. Tumors were observed in some animals.

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[2] The rebuttals and comments were reviewed by the Criteria and Evaluation Division (CED) of the Office of Pesticide Programs (OPP), the EPA Cancer Assessment Group (CAG), and/or two consulting firms. These reviewers extracted items from the rebuttal submissions which specifically and authoritatively addressed the risk data upon which the presumption against chlorobenzilate was based. The reviewers did not analyze testimonials and other comments not supported by data or references. The reviewers evaluated rebuttal items as they related to the risk information and submitted their comments and conclusions to the Agency Working Group on chlorobenzilate.

Respondents argued, among other things, that too few animals were examined histopathologically for proper statistical analysis. For example, although 80% of the male control animals survived, tissues were studied from only 25% of the survivors. Agency consultants reevaluated the use of this data to demonstrate oncogenic effects and reported that too few animals were examined histopathologically, that tumor incidence in the control groups was often greater than in the experimental groups, and that examination of only representative animals and tissues may have biased the results (Freudenthal and Leber, 1977; Savage and Hayes, 1977). The Agency agrees that these factors indicate that the data may not be reliable indicators of oncogenicity.

b. Woodard (1966)

The Ciba-Geigy Corporation, a chlorobenzilate registrant, had the Woodard Research Corporation conduct a study in which rats were given chlorobenzilate in the diet. Registrants, including Ciba-Geigy, contended that the tumor incidence in the control animals was often higher than the treated animals, that the investigators failed to conduct necropsies of animals that died before the scheduled end of the study, and that they failed to examine histopathologically an adequate number of animals. For example, no more than 20% of the control and test animals from each group were histopathologically examined. Agency consultants confirmed that the studies were defective in these respects and that the data were unreliable for assessing the oncogenicity of chlorobenzilate (Freudenthal and Leber, 1977).

These consultants also reported that there was an increased incidence of liver tumors at the highest dose level which, although not statistically significant, indicated the need for further study. Since the Innes and NCI studies provided reliable data on chlorobenzilate-induced liver tumors in rodents, data in this study are consistent. However, the Agency agreed with the consultants' conclusion that these data alone do not indicate that chlorobenzilate is an oncogen.

2. Unsuccessful Rebuttal Arguments

a. Innes et al (1969)

Innes et al. tested the tumorigenicity of 120 pesticides and industrial compounds by continous oral administration to two hybrid strains of mice. Tumors of the liver were observed in 52.9% (9/17) of the male mice ingesting 603 ppm chlorobenzilate compared with 10.1% (8/79) of the control animals. Liver tumors were not observed in the females. These data are detailed in Table 7, Subsection II,C. This section summarizes the rebuttals of the Innes study and the Agency's response.

i. Criticisms Relating to Experimental Design and Methods

Size of Test Groups: Registrants argued that only 18 male and 18 female mice were fed chlorobenzilate, and that this was too few mice to permit a valid statistical analysis [Alikonis, 1976a, 1976b, 1976c (23-25:30000/3)].[3/] The Agency acknowledges that the number of animals

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[3/] The names and numbers in parentheses identify the source of each rebuttal in terms of the signer, date, and EPA identification number.

in a study does limit the sensitivity of the test, but notes that in the Innes study an appropriate proportion of the animals were autopsied and that both chlorobenzilate-treated groups of F hybrid male mice demonstrated a statistically significant increase ($p \leq 0.02$) in animals with tumors compared to controls (Freudenthal and Leber, 1977). The Agency also notes that the Mrak Report concluded that the number of animals per group in the Innes study was sufficiently large to provide a sound basis for statistical analysis of the results.

Some registrants noted that the Innes study was a mass screening study which involved many chemical compounds and few animals and that, in the introduction, the authors urged against drawing conclusions from the study without confirmatory research (Jovanovich, 1976a [1:30000/3]; Alikonis, 1976a, 1976b, 1976c [23-25:30000/3]). These considerations do not negate the statistically significant ($p < 0.001$) increase of hepatomas in chlorobenzilate-treated male mice (Freudenthal and Leber, 1977). In computing significance, sample size is necessarily considered. Further, the Mrak Commission referred to the Innes study as a "fine-mesh screen designed to identify as many as possible of the carcinogens submitted to it," and concluded that it "performed this task with considerable success." Moreover, an analysis of the results of the recent NCI study confirm that chlorobenzilate is oncogenic (Barton, 1977).

Choice of Strains: Registrants argued that the two first generation hybrid strains of mice used by Innes et al. did not have the genetic heterogeneity of normal animals and, therefore, should not be used in cancer research. They noted that randomly bred animals are recommended by the Mrak Commission, the Food and Drug Administration Panel on Carcinogenesis in 1971, and the World Health Organization in 1961 [Balser, Jovanovich, 1976b (20:30000/3); Jovanovich, 1976 (31:30000/3)]. However, the Agency has concluded that the hybrid mice used in this study were suitable test animals. A low incidence of tumors appeared in control groups, and the strain was highly susceptible to induction of tumors by positive control chemicals (HEW, 19699. While randomly bred animals are preferred by some scientists, true random breeding is difficult to achieve in practice and results in broad, ill-defined gene pools. Moreover, inbred strains have been described as the best means for investigating chemical carcinogenesis (Goldberg, 1974).

Assignment of Littermates to the Same Group: Registrants argued that the assignment of littermates to the same experimental groups was inappropriate [Jovanovich, 1976a (1:30000/3); Murphy, 1976a (22:30000/3)]. The Mrak Commission reported that when the Innes data were reanalyzed under a more rigorous statistical procedure to take this possible bias into account, the differences reported as statistically significant in the original study remained significant (HEW, 1969).

Treatment of Newborns and Route of Administration: Registrants stated that the FDA criteria for cancer testing recommend that newborns not be included in cancer tests [Balser, Jovanovich, 1976b (20:30000/3); Alikonis, 1976a, 1976b, 1976c (23-25:30000/3)]. Specifically, the Innes study was faulted for beginning to administer chlorobenzilate when the mice were 7 days old. Registrants argued that the immune system in these very young animals is incompletely developed, rendering them more susceptible to the development of tumors. The registrant cited the FDA guidelines which state, "This might be a satisfactory screening procedure under limited conditions but cannot be recommended as a routine test procedure" (FDA, 1971).

The Agency has rejected this argument because young and more suscpetible animals are used in oncogenicity studies to optimize detection of oncogenic activity. In addition, when a relatively small number of animals is used in feeding studies, it is appropriate to increase the sensitivity of the experiment with this technique. This approach is explained in the NCI Guidelines for Carcinogenic Bioassays in Small Rodents (Sontag et al. 1976) which state that chronic study animals should be weanlings, if possible, since a poorly developed immune system may sensitize these animals to carcinogens and make them more susceptible. Human infants also exhibit a weak immune response.

One registrant contended that the administration of chlorobenzilate to infant mice by gavage flawed the study [Jovanovich, 1976a (1:30000/3)]. Gavage is an accepted means of administering a test material to animals, especially to young animals or when an exact oral dose is required (Wilson, J.G., 1973; Goldberg, 1974).

Pathogen-Free Animals: With reference to the FDA guidelines (FDA, 1971), one registrant stated, "Specific pathogen-free animals should be avoided because of possible increased susceptibility to infection" [Balser, Jovanovich, 1976b (20:30000/3)]. The FDA's recommendation is intended as an experimental design measure to safeguard against early deaths from infection; reductions in the number of animals surviving a long-term study would result in a less valid study. Since there was a high survival rate among the animals in the Innes study and no data indicating that there was significant infection, the FDA precaution is not relevant in this case.

ii. Criticisms Relating to Pathological Diagnoses

One registrant argued that, since most of the animals in the Innes study did not die of cancer but were sacrificed at the end of the study, chlorobenzilate is not a potent carcinogen [Balser, Jovanovich, 1976b (20: 30000/3)]. Agency regulations which authorize the rebuttable presumption review provide that a presumption will arise if a chemical is oncogenic, or tumor-producing. Such tumors need not cause the death of the animals.

One registrant stated, "Many of the cancers are detected only by microscopic examination" in the Innes study [Balser, Jovanovich, 1976b (20:30000/3)] and concluded that chlorobenzilate should not be considered an oncogenic risk. Diagnosis of tumors by microscopic examination of histological preparations is essential to a complete review of the effect of a chemical on tissues. The risk criterion provides that a rebuttable presumption shall arise if a compound is oncogenic; there is no requirement that tumors be macroscopically detectable.

One registrant argued that chlorobenzilate should not be considered an oncogenic risk since tumors found in the Innes study had not generally metastasized [Balser, Jovanovich, 1976b (20:30000/3)]. The EPA "Interim Guidelines for Carcinogen Risk Assessment" (41 FR 21404, May 25, 1976) specify that:

> Substantial evidence [that an agent is a human carcinogen] is provided by animal tests that demonstrate the induction of malignant tumors in one or more species including benign tumors that are generally recognized as early stages of malignancies.

Because diagnoses of cancer can be made only by expert pathologists, several registrants have concluded that the evaluations of the Innes study are subjective [Balser, Jovanovich, 1976b (20:30000/3); Alikonis, 1976a, 1976b, 1976c (23-25:30000/3)]. The Agency acknowledges that pathologic diagnosis is a special skill and relies on the known ability of the pathologists who reviewed the Innes study slides. The independent diagnoses of the pathologists who reevaluated the slides add considerably to the Agency's confidence in this judgment.

One registrant cited FDA's 1971 Criteria for Cancer Testing (FDA, 1971) which recommended, "It is desirable that both gross and microscopic examinations be conducted without knowledge of the treatment of specific animals." The registrant argued that the pathologists who reevaluated the Innes study slides would know the treatments prior to examining the slides [Balser, Jovanovich, 1976b (20:30000/3)]. The registrants have not submitted any specific information that would cause the Agency to doubt the validity of the observations of the pathologists who reevaluated these slides. The pathological evaluations were performed through a "blinded" evaluation of the tissue preparations of unknown origin. This procedure precludes the possibility of the suggested bias, regardless of whether or not the pathologists knew the experimental protocol.

One registrant contended that EPA demonstrated its lack of confidence in the Innes study when the Agency's Toxicology Branch, Registration

Division (RD), refused to accept data from this study as evidence that certain other chemicals were not oncogenic [Murphy, 1976a (22:30000/3)]. The refusal of RD to accept the fact that some Innes study data demonstrated that some chemicals are not carcinogenic does not conflict with the acceptance of data relating to chlorobenzilate. Specifically, since chemicals tested in this study were not administered throughout the entire lifetimes of the animals and since a small number of animals was tested, conditions were not optimum for tumor detection, and therefore there are bases for questioning negative findings.

b. NCI (1977)

A summary of the final individual animal pathology data was provided by NCI on January 27, 1977 (NCI, 1977). NCI tested the oncogenicity of chlorobenzilate in B6C3F1 mice and Osborne-Mendel rats. Neither sex of rats showed statistically significant responses. The incidence of hepatocellular carcinomas in male mice was 68% (32/47) at 4,000 ppm and 49% (22/45) at 6,000 ppm, compared to 24% (4/17) in the control group. These tumors were observed in 23% (11/49) of the female mice ingesting 3,200 ppm and 26% at 6,400 (13/50), compared to 0% (0/20) in the control group. An EPA analysis indicates that the chlorobenzilate-treated mice showed statistically significant increases in the number of total tumors and heptatocellular carcinomas at $p = 0.017$ and $p = 0.0001$, respectively (Barton, 1977a).

i. NCI Appraisal of Results

Registrants submitted a letter from the Chief of the Carcinogen

Bioassay and Program Resources Branch, NCI, which stated that "the compound appears not to be carcinogenic to mice and rats of both sexes" [Jovanovich, 1976a (1:30000/3); Murphy, 1976a (22:30000/2)]. The letter refers only to a preliminary inspection of unverified data as of May 13, 1976, and does not necessarily reflect the final NCI interpretation of the data. EPA's analysis of the verified histopathology report of January 27, 1977, indicates a statistically significant ($p = 0.017$) increase in total tumors for mice of both sexes fed chlorobenzilatd (Barton, 1977a). NCI has not yet completed their analysis of this final data.

ii. Arguments Relating to Control Animals

The occurrence of tumors in the control group was not the same as the overall incidence usually observed in untreated mice of this strain. One registrant argued that if the incidence of tumors in the treated mice were compared to the historical baseline incidence of tumors in this strain, the difference in tumor occurrence would not be statistically significant (Murphy, 1976a [22:30000/3]). NCI reports that the historical incidences of spontaneous primary liver tumors in untreated male and female B6C3F1 mice are 15.6% and 2.5%, respectively; the comparable rates for concurrent controls in the study were 23.5% and 0%. The Agency's Cancer Assessment Group (CAG) advised that because this difference is negligible for a sample size of 20 control animals, the historical control data does not appreciably affect the significance of the chlorobenzilate findings (Albert, 1978).

Citing the World Health Organization's (WHO) recommendations, one registrant claimed that the control group should have contained 70 animals [Balser, Jovanovich, 1976b (20:30000/3)]. The control group contained only 20 mice although the treatment groups contained 50 mice each. CAG evaluated this rebuttal and the WHO guidelines, and pointed out that there should have been 35 animals in each test group to provide optimal statistical efficiency (Anderson, 1977). It was emphasized, however, that even though the test was not as sensitive as it could have been, a statistically significant elevation in tumor incidence was found (Barton, 1977a).

One registrant argued that, since only 60% of the male mice in the control group survived to the end of the study, meaningful statistical evaluation of the study was not possible [Balser, Jovanovich, 1976b (20: 30000/3)]. The statistical analysis was based on the animals that survived and were examined histopathologically. The survival rate in the controls was better or the same as that of the low dose group to which it was compared. This comparison is shown in Table 2. As a result the significant "p" value is not biased by better test group survival. Using the Fishers

TABLE 2. Survival Rates for Animals Examined Histopathologically (NCI, 1977)

Week of Study	Control Group	Low Dose Group
48	1.000	0.979
50	0.941	0.915
51	0.941	0.872
56	0.941	0.851
63	0.941	0.830
68	0.941	0.809
69	0.941	0.787
72	0.882	0.787
73	0.824	0.787
74	0.765	0.787
77	0.765	0.766
86	0.765	0.745

exact 2 x 2 test, the "p" value is less than 0.002, which indicates that the differences in tumor incidence observed between treated and control animals were highly significant (Anderson, 1977).

iii. Variable Dose Levels

One registrant pointed out that dose levels varied accoring to the age and sex of the animals [Balser, Jovanovich, 1976b (20:30000/3)]. The dosing regimen was selected on the basis of preliminary tests to determine maximum tolerated doses. Standard procedure for selecting dosage levels permits variation according to sex. In addition, food intake relative to body weight can vary with age; thus, an adjusted concentration of the chemical in the diet to accommodate for this is solid experimental procedure (Mishra, 1977; Edwards, 1977).

c. Other Arguments Against the Innes and NCI Studies

One registrant argued that neither Innes nor NCI adhered to all FDA criteria for carcinogenicity testing (FDA, 1971), but did not note specific inconsistencies in the NCI study (See Section II,A,2,a, for Innes inconsistencies). Although the FDA criteria were developed to test methods and to provide a sensitive screen for cancer-causing agents, deviation from these guidelines does not alone invalidate a study. In this case, since both the NCI and Innes studies showed statistically significant increases in tumors in mice, the studies were clearly sensitive enough to detect oncogenic activity.

Another argument was that the secondary toxic effects noted in these studies made pathological evaluation difficult [Balser, Jovanovich, 1976b

(20:30000/3); Alikonis, 1976a, 1976b, 1976c (23-25:30000/3)]. While secondary toxic effects may complicate the diagnosis of tumors, the registrants have offered no evidence which casts doubt on the validity of the pathologists' conclusions in these studies.

Several registrants contended that the Agency's presumption of chlorobenzilate's oncogenic risk was based on false positive results from both Innes and NCI studies [Jovanovich, 1976c (31:30000/3)]. No data were offered to support this argument, and based on both studies, the probability of false positive results for the increase of tumors in chlorobenzilate-treated mice was very slight (Barton, 1977).

Several registrants argued that data from the Innes and NCI studies were unreliable because inbred strains may carry tumor-causing viruses. These registrants maintained that the tumors found in these studies were similar to those produced by viruses [Balser, Jovanovich, 1976b (20:30000/3); Alikonis, 1976a, 1976b, 1976c (23-25:30000/3); Jovanovich, 1976c (31:30000/3)]. This argument was rejected for two reasons (Mishra, 1977). First, although the association of viruses (or C-type particles) and the development of tumors in test animals has been demonstrated, no causal relationship has been established. Second, even if viruses in mice were oncogenic, the control animals used in both tests showed markedly fewer tumors than the chlorobenzilate-tested animal.

d. Other Arguments

i. Other Cancer Tests

One registrant [Murphy, 1976a (22:30000/3)] cited a 1965 Hazelton

Laboratories' study in which chlorobenzilate was fed at levels of 0, 100, 500, and 3,000 ppm active ingredient to six beagle dogs. No evidence of oncogenic activity was observed. However, the animals were exposed to chlorobenzilate for only two years, which is generally too short a portion of the dog's life span for the development and detection of tumors. It is generally accepted that in an oncogenic bioassay, a test agent should be administered continuously for the larger part of an animal's life span to achieve "greatest confidence" in a negative result. This translates to a test duration of 7-10 years for carcinogenicity tests in dogs (Page, 1977).

ii. Negative Mutagenicity Testing

Two registrants referred to the frequently observed correlation between mutagenic and oncogenic activity and cited data which suggested that chlorobenzilate is not mutagenic and, therefore, not oncogenic [Murphy, 1976a (22:30000/3); Alikonis, 1976d (33:30000/3)]. This argument can be rejected for two reasons. First, mechanisms other than mutation may cause cancer. Second, although there is a high correlation for some classes of chemicals between carcinogenicity in mammalian test systems and mutagenicity in certain microbial systems, this correlation is not perfect, and false positive and false negative indications do occur. For instance, the reversion assay in Salmonella with metabolic activation , i.e. the Ames test, has a high "false negative" correlation for chemical classes such as cyclodienes, chlorinated hydrocarbons, and certain metals. For these classes of compounds the Ames test is often negative, although there are positive results in mammalian bioassays for carcinogenicity. Chlorobenzilate falls into the potentially "false negative" group of chemicals (Pertel, 1977). For these reasons the negative results in the in vitro test battery submitted in rebuttal of the carcinogenicity of chlorobenzilate are not convincing (Pertel, 1977;1978).

iii. Lack of Exposure Necessary to Cause Adverse Effects

Two registrants concluded that even if chlorobenzilate were carcinogenic, the human exposure would not be high enough to pose any risk [Murphy, 1976a (22:30000/3); Murphy 1976b (22:30000/3)]. The exposure estimates in Section II,B, of this document and the risk estimate in Section II,C, in the Agency's judgment, indicate that humans may be exposed to amounts of chlorobenzilate which may cause sufficient adverse effects to require the Agency to consider whether uses of chlorobenzilate offer offsetting social, economic, or environmental benefits.

iv. Epidemiological Data

A preliminary company report on chlorobenzilate manufacturing epidemiology [Murphy, 1976a (22:30000/3)] was submitted to show that no unusual health problems had been detected among employees of a chlorobenzilate production facility in Albama. The study was determined to be inconclusive (Rossi, 1978), and was not further considered. No other reliable epidemiological data is currently available.

3. Adverse Testicular Effects in Rats

The studies on which the presumption against chlorobenzilate was based include data indicating that chlorobenzilate has adverse effects on the testes of rats. The Agency did not review these data in its RPAR notice and the registrants were not invited to comment in their rebuttals. However, in reevaluating chlorobenzilate studies in connection with the RPAR review, the Agency concluded that the testicular effects' data also required consideration. Re-examination of these studies disclosed that testicular toxicity in rats has been reported in five of the studies examined.

Horn et al. (1955) in a two-year study using 50 and 500 ppm, found a dose-related increase in the number of small and/or soft testes among the survivors of the study. Compared with 25% (4/16) of the controls, at 50 ppm chlorobenzilate, 69% (9/13) of the male rats evidenced testicular effects, and at 500 ppm chlorobenzilate, 100% (14/14) showed these effects.[4] In a 2-year study using 40, 125 and 400 ppm, Woodard (1966)[4] found, among the animals examined, more frequent testicular changes at 125 ppm and 400 ppm than in the controls or at 40 ppm. At 125 ppm, 33% (2/6) of the animals evidenced change and at 400 ppm, 60% (3/5) compared with 0% (0/5) in the controls and with 20% (1/5) at 40 ppm. A dietary level of 40 ppm was considered the no-effect level in this study.

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[4] The rebuttable presumption against chlorobenzilate was based in part on oncogenicity data presented in this study, and the Agency has concluded that respondents sucessfully rebutted these data as to the oncogenic presumption. However, these rebuttal arguments do not apply for all purposes and independent analyses of the testicular effects' data is appropriate.

A two-year study by NCI (1977), in which rats were fed 1,600 or 3,200 ppm for 78 weeks, reported an increased incidence of abnormal testicular pathology among treated males. Sixty-six percent (33/50) evidenced adverse effects at both the high and low doses compared with 18% (9/49) of the controls. Testicular atrophy was the most commonly observed effect. Further, in a 99-day subacute study using 20,100, 500, and 2,500 ppm, spermiogenetic injury and atrophy of the gonads were found in 25% (5/20) of the rats at the highest dose level. In this study, 500 ppm was judged to be the no-effect level (Potrepka, 1978a). In a 3-generation study in which F_O rats were fed 50 ppm and subsequent generations fed either 25 or 50 ppm, Woodard (1966) found decreased testicular weights in F_{1b} males. At 25 ppm, mean testicular weight was reduced to 3.04 g and at 50 ppm, significantly reduced ($p = 0.05$) to 2.75 g compared with 3.24 g in the controls (Quaife, 1966).

Chlorobenzilate studies using other species are limited, and those that are available generally do not contain comments on testicular changes. In a review of slides from the Innes study on mice, one pathologist indicated that there might be a treatment-related increase in testicular atrophy. These data could only be considered suggestive because of the limited number of samples studied (Frith, 1976). Testicular effects were not reported for mice in the NCI study.

The biological significance of the adverse testicular effects has not been established. Although the reproduction study examined did not disclose significant differences in fertility between treated and untreated animals, the regular occurrence of testicular atrophy in animals exposed to chlorobenzilate warrants concern. Since none of the other studies were designed to measure reproductive capacity or testicular function, the reproductive and physiological significance is unknown. Consistent with its obligation to protect human health, the Agency must assume that the data (showing chlorobenzilate-induced injury to the testes) indicates that chlorobenzilate may also interfere with the endocrine or spermatogenic function of this organ, in the absence of data establishing that no such interference occurs.

B. Exposure Analysis

Registrants, the U.S. Department of Agriculture, and other sources provided data on patterns of chlorobenzilate use which the Agency has used to identify populations which may be exposed to chlorobenzilate and to estimate the extent of exposure.

1. Dietary Exposure

The Agency's estimates of human dietary exposure are based on residue data and the extent to which chlorobenzilate is used on each of the food crops for which it is registered. A reasonable upper limit of the dietary exposure of the general U.S. population was calculated, based on the average individual's consumption of commodities, including orange juice, produced from crops treated with chlorobenzilate (Severn, 1978). Because there were no detectable residues in most of the edible portions of these foods, these sources were assumed to contain 0.1 ppm, which is the limit of detection in the analytical method used to measure representative samples (FDA, 1971). Accordingly, the calculations presented in

Table 3 may be regarded as reasonable upper limit estimates.[4/] In addition, since apples and pears are eaten whole, residues in these crops were estimated at 5 ppm, the established tolerance level. Finally, although chlorobenzilate-treated citrus is processed into other products, e.g. citrus oil, which may also be sources of dietary exposure, data for estimating exposure from these sources were not available (See Section IV, Option E).

Florida residents may ingest additional significant amounts of chlorobenzilate because pulp from chlorobenzilate-treated citrus fruit is fed to dairy and beef cattle which are raised and marketed in Florida, although a limited EPA survey of Florida milk samples detected no residues at the 20 ppb detection limit (TSD, 1978).

Formica, et al. (1975) reported that on days 1 thorough 42 during which cows were fed pulp to which 20 ppm chlorobenzilate had been added, chlorobenzilate levels in milk ranged from 0.03 ppm to 0.04 ppm. EPA also completed a limited survey of Florida citrus pulp-mixed feed and found that the chlorobenzilate content averaged 0.16 ppm (TSD, 1978). Other pulp data FDA, 1976 and proprietary data (Reed, 1978d) indicate that chlorobenzilate can occur at 2 ppm in citrus pulp fed to cattle. Based on these data, the Agency has estimated that chlorobenzilate may be present in milk at 1 to 3 ppb (Reed, 1978c). This level could not be detected by the current FDA

[4/] The Agency's estimates of exposure and risk are based on the data, information and assumptions cited for each estimate. In many cases, a range of values or several reasonable assumptions, tested or untested, are appropriate for the analysis. The Agency generally selects values and assumptions which permit a conservative (from the standpoint of protecting the public health) risk estimate rather than using average values or generalized assumptions.

Table 3

REASONABLE UPPER LIMIT OF DIETARY EXPOSURE TO CHLOROBENZILATE

U.S. Population Exposure

Commodity	Consumption (g/day)[a]	Extent of Use by Crop (%)[b]	Assumed Maximum Residue (ppm)[c]	Maximum Ingestion (ug/day)
Citrus:				
Oranges (inc. juice)	42.00	47.80	0.1	< 2.01
Grapefruit	19.30	60.90	0.1	< 1.18
Other Citrus	12.70	31.00	0.1	< 0.40
Other Fruit:	55.20	0.08	5.0[d]	< 0.21
Nuts:	1.18	3.60	0.1	< 0.0043
Total U.S.				< 3.8 (0.002 ppm)
		[Percent with Potential Occurrence][f]	[e]	
Beef and Lamb	143.2	10	0.04	< 0.57
Milk	184.7	100	0.0024 - 0.04	< 0.44 - < 7.39
Total Florida Additional				< 1.01 - < 7.96
Grand Total Florida				< 4.81 - < 11.76 (< 0.0025 - < 0.0061 ppm)

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[a] Severn, 1978

[b] Doane, 1976

[c] Detection level in the most representative sampling

[d] Tolerance level

[e] Feeding by-products of citrus processing (pulp and molasses) to cattle in Florida is viewed as an indirect dietary source of chlorobenzilate. It results in additional dietary exposure for the Florida population.

[f] Based on limited EPA survey (Luttner and McWhorter, 1978)

monitoring method. However, because these data are inconclusive, a range has been expressed (Table 3) up to 40 ppb which would be the maximum theoretical occurrence (Reed, 1978a). In addition, based on the Mattson and Insler study (cited in Severn, 1978), the Agency estimated that chlorobenzilate may be present at 0.04 ppm in beef (Table 3).

2. Occupational Exposure

Ground applicators and citrus pickers are exposed to chlorobenzilate through its use on citrus crops. The USDA estimates that the current use of chlorobenzilate in ground application on citrus is carried-out by as few as 714 applicators for 30 to 40 days per year or by as many as 1375 applicators for 10 to 20 days per year (Severn, 1978). The worst case, which is represented by 714 applicators for 40 days per year, is shown in Table 4A. No data is available to indicate the actual amounts of chlorobenzilate exposure to these applicators; however data on exposure to ground applicators during application of other pesticides (Wolfe, et al.1967) was used to estimate these amounts at between 120 mg and 440 mg dermally and 1 mg by inhalation during each day of application. Since similar pesticides are known to be absorbed through the skin at a rate of only about 10% (Feldmann and Maibach, 1974), the daily dermal dose range was estimated to be 12 to 40 mg; Feldman and Maibach assumed that pesticides which are inhaled are absorbed 100%. Thus, the total daily dose for ground applicators was estimated at 13 mg to 41 mg. Assuming up to 40 years of occupational exposure to chlorobenzilate, the average daily dose ranged from 0.81 mg to 2.57 mg. For purposes of relating this estimated exposure to the animal dose-response data, the average daily dose is expressed as 0.39 ppm to

1.3 ppm dietary equivalents (Table 4).[5/]

There are approximately 25,000 to 30,000 citrus pickers who may be occupationally exposed to chlorobenzilate, but there is too little data available at this time to permit a estimate of exposure and potential risk. Since citrus pickers work in the groves after the pesticide is applied, the Agency has assumed that their exposure is less than the applicators' exposure. The Agency has also assumed that surface chlorobenzilate residues on fruit and foliage surfaces may be a primary source of contact exposure. If citrus pickers are exposed to the pesticide in this manner, an exposure estimate could be based on residue data together with the 10% dermal absorption and 40-year duration figures used in estimating applicator exposure (See Section IV, Option E).

3. Other Potential Exposure

Chlorobenzilate is registered for aerial application to citrus for the control of citrus rust mites. This manner of application could result in drift, depending on the speed of the wind and the size of the

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[5/] The applicator exposure estimate is based on amounts of chlorobenzilate to which applicators may be exposed through the skin and through lung absorption during pesticide application. In this case, the values range from 0.81 to 2.57 mg/day. However, since the risk estimates (See Section II,C) are based in part on animal test data derived from dietary exposure, reported as ppm/day, the human exposure and the animals' exposure are not expressed in the same terms. Therefore, for purposes of relating the animal dose-response data which is expressed in ppm to the human exposure data which is calculated initially as mg/day, the latter has been converted to dietary equivalents (Albert, 1978).

Table 4

CHLOROBENZILATE

OCCUPATIONAL EXPOSURE

GROUND APPLICATORS (AGRICULTURAL-CITRUS ONLY)

Maximum Extent of Exposure (Absorbed[a]/day)
Inhalation - 1 mg/day
Dermal - 12-40 mg/day

Duration of Exposure
Assumption - 40 days/year for 40 years

Reasonable Upper Limit of Exposure - (0.39 to 1.3 ppm)(Dietary Equivalents)[b]

Maximum Number of Ground Applicators at This Level of Exposure - 714 spray droplets. In this way there could be exposure to people near the vicinity of application. However, there is no data on which to base an estimate of the magnitude of the potential exposure in this situation.

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[a] Adapted from Wolfe, et al. (1967) data on similar pesticides (Severn, 1978)

[b] Daily amount, time-weighted on duration of exposure (Thorsland, 1978)

C. Risk Assessment

1. Risk: Oncogenic Effects

The chlorobenzilate cancer risk assessment is based on the principles and procedures outlined in the EPA cancer risk assessment guidelines (41 FR 21402, May 25, 1976). These guidelines specify that a substance will be considered a "presumptive cancer risk when it causes a statistically significant excess incidence of benign or malignant tumors in humans or animals," that current and anticipated exposure levels are appropriate considerations, and that cancer risk estimates may be derived from a variety of risk extrapolation models such as the log-prohibit and linear non-threshold models.

In accordance with these principles, the EPA Cancer Assessment Group (CAG) (Albert,1978), and Agency consultants (Felkner and Lombardini, 1978) developed risk estimates using several different models and a range of exposure estimates. CAG has concluded that "...the weight of evidence indicates that chlorobenzilate is a possible human carcinogen" (Albert, 1978). After reviewing the data sources and the preliminary risk estimates, CAG concurred in recommendations that the final risk estimates be based on data from the Innes study using the one-hit model (Table 5) (Albert, 1978).[6/] CAG and the consultants recommended using the Innes rather than the NCI data because the oncogenic response per unit of dose of chlorobenzilate

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[6/] CAG has reviewed risk according to the NCI data (Albert, 1978b).

Table 5

INNES DATA[a] USED TO ESTIMATE RISK

Strain	Dose (ppm)	Incidence Hepatomas Male		Female	
"X"	0	8/79	(10.1%)[b]	0/87	(0%)
	603	9/17	(52.9%)	0/18	(0%)
"Y"	0	5/90	(5.6%)	1/82	(1.2%)
	603	7/17	(41.2%)	0/18	(0%)

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[a] This was an eighteen-month feeding study on two hybrid strains of mice. "Strain X" = (C57BL/6 x C3H/Anf)F_1; "Strain Y" = (C57BL/6 x AKR)F_1, Innes et al., Journal of the National Cancer Institute, 42:1101-1114, 1969

[b] Used to estimate risk

in the Innes study was 5 times greater (Albert, 1978). CAG explained that animals in the Innes study were fed the compound beginning at a younger, more susceptible age. In addition, CAG concluded that the Innes study data were more appropriate for the risk calculations because the human response is more likely to be similar to the most sensitive animal species and because of the possibility that people will be exposed to chlorobenzilate as infants.

Human risk is defined mathematically as the probability that an individual exposed to chlorobenzilate will develop a tumor due to that exposure during his or her lifetime. To develop a risk estimate, CAG and Agency consultants evaluated the animal test data and the human exposure data using several different models. They selected the one-hit model as providing the most conservative estimate.[7] This model relates the probability of the development of tumors in humans to the exposure and animal test data as follows:

$$\text{Risk} = 1 - e^{-(Bx)}$$

$$B = (1/y)/\ln\,[1/(1-P)]$$ [8]

Where:

B = slope coefficient of the one-hit model
$P = (Pt-Pc)/(1-Pc)$
Pc = Incidence of hepatomas in control animals
Pt = Incidence of hepatomas in test animals
y = Test animal exposure (ppm)
x = Potential human exposure (ppm)

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[7] The linear and one-hit models were both used to calculate risk potential (Felkner, 1978). However, the one-hit model projected the most risk and was therefore chosen as the more conservative basis of projecting potential risk from the Innes data. The Log-Probit model was considered inappropriate for estimating risk from the results of the Innes study (Felkner, 1978).

[8] The slope B can be derived from the general expression for the one-hit model which is: $\text{risk} = 0 + (1-0)(1-e^{-Bx})$ where 0 is the probability of developing the tumor due to causes other than the deliberatly added chemical.

The risk estimates are summarized in Tables 6, 7, and 8.

2. Risk: Adverse Testicular Effects

The primary routes of exposure to chlorobenzilate are in the diet and during spray application. The following estimates are based upon analyses by the Criteria and Evaluation Division.

a. Dietary Exposure

As previously determined, the average human exposure to chlorobenzilate from the diet is 0.0038 mg/day for the general population and 0.0095 mg/day for the Florida population (Severn, 1978). For a 70 kg male, this converts to daily dietary equivalents of 0.002 ppm for the general population and < 0.006 ppm for the Florida group.[9/] Because human exposure from the diet is a lifetime possibility, it is appropriate to use a whole life feeding model for risk calculations. Comparing the estimated exposures to a no-observable effects level (NOEL) of 40 ppm (See Section II,A,3), indicates that the margin of safety is approximately 15,000 for men exposed to chlorobenzilate in the diet (Potrepka, 1978a).

b. Occupational Exposure

Maximum exposure to unprotected spray applicators has been estimated to be 13 to 41 mg/day (Table 4). A direct comparison between applicator exposure and a NOEL based on daily exposure over an entire life span may not be appropriate because of the non-continuous nature of applicator exposure;

9/ See Footnote 5.

Table 6

CHLOROBENZILATE

POTENTIAL OCCUPATIONAL CANCER RISK

GROUND APPLICATORS (AGRICULTURAL - CITRUS ONLY)[a]

	Maximum[b] Lifetime Probability of Tumor Formation (Less Than)	Maximum[c] Mathematical Expectation of Numbers of Tumors During a Lifetime (Less Than)
One-hit Model (NCI Data)[d]		
Observed	80 to 300 in 1 million	0.1 to 0.2
One-hit Model (Innes Data)[e]		
Observed[f]	400 to 1400 in 1 million	0.3 to 1.0

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[a] There is insufficient data to allow estimates of risk to aerial applicators, non-citrus applicators or harvesters of the treated crops.

[b] Assumes that ground applicator's daily dietary exposure to chlorobenzilate is 0.39 to 1.3 ppm. The one-hit model is a conservative technique for projecting risk from laboratory animals to man.

[c] Since lifetime animal studies were used to make risk estimates, the probability of cancer in humans is estimated as a lifetime probability, and should, therefore, be interpreted as an index or "mathematical" expectation rather than a "clinical" expectation.

[d] In addition to normal spontaneous rate; estimate based on NCI study male mice with hepatocellular carcinomas [32 out of 48 (treated); 4 out of 19 (controls)] (Albert, 1978b).

[e] In addition to normal spontaneous rate; estimate based on Innes Study "Strain X" male mice with hepatomas [9 out of 17 (treated); 8 out of 79 (controls)] (Albert, 1978).

[f] Estimate used.

Table 7

CHLOROBENZILATE

POTENTIAL CANCER RISK THROUGH DIETARY EXPOSURE

FLORIDA POPULATION (8,000,000)

	Maximum[a] Lifetime Probability of Tumor Formation (Less Than)	Maximum[b] Mathematical Expectation of Numbers of Tumors During a Lifetime (Less Than)
One-hit Model (NCI Data)[c]		
Observed	0.5 to 1.2 in 1 million	4 to 10
One-hit Model (Innes Data)[d]		
Observed[e]	2.7 to 6.5 in 1 million	22 to 52

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[a] Assumes that dietary exposure occurs at the level of exposure expressed as reasonable upper limit (0.0025 to 0.0061 ppm daily throughout lifetime), and model projects conservative expression of risk.

[b] Since the animal study was conducted throughout lifetime exposure, the chance of cancer occurrence is extrapolated as the potential of a cancer event during a lifetime, and should, therefore, be interpreted as an index or "mathematical" expectation rather than a "clinical" expectation.

[c] In addition to normal spontaneous rate; estimate based on NCI study male mice with hepatocellular carcinomas [32 out of 48 (treated); 4 out of 19 (controls)] (Albert, 1978b).

[d] In addition to normal spontaneous rate; estimate based on Innes study "Strain X" male mice with hepatomas [9 out of 17 (treated); 8 out of 79 (controls)] (Albert, 1978).

[e] Estimate used.

Table 8

CHLOROBENZILATE

POTENTIAL CANCER RISK THROUGH DIETARY EXPOSURE

U.S. POPULATION (EXCEPT FLORIDA)(212,000,000)

	Maximum Lifetime Probability of Tumor Formation (Less Than) [a/]	Maximum [b/] Mathematical Expectation of Numbers of Tumors During a Lifetime (Less Than)
One-hit Model (NCI Data) [c/]		
Observed	0.4 in 1 million	86
One-hit Model (Innes Data) [d/]		
Observed [e/]	2.1 in 1 million	445

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a/ Assumes that dietary exposure occurs at the level of exposure expressed as reasonable upper limit (0.0025 to 0.0061 ppm daily throughout lifetime), and model projects conservative expression of risk.

b/ Since the animal study was conducted throughout lifetime exposure, the chance of cancer occurrence is extrapolated as the potential of a cancer event during a lifetime, and should, therefore, be interpreted as an index or "mathematical" expectation rather than a "clinical" expectation.

c/ In addition to normal spontaneous rate; estimate based on NCI study male mice with hepatocellular carcinomas [32 out of 48 (treated); 4 out of 19 (controls)] (Albert, 1978b).

d/ In addition to normal spontaneous rate; estimate based on Innes study "Strain X" male mice with hepatomas [9 out of 17 (treated); 8 out of 79 (controls)] (Albert, 1978).

e/ Estimate used.

similarly, use of a NOEL from a subacute study does not consider the fact that applicator exposure may be repetitive over most of the life span. Assuming the analysis employed in the estimation of oncogenic risk adequately adjusts for the difference between continuous and repeated exposure, a dietary equivalent of 0.39 to 1.3 ppm would be derived for a 70 kg man (Albert, 1978).

Based upon a NOEL of 40 ppm, the margin of safety for unprotected spray applicators would range from 55-169. The values given for margin of safety were calculated based upon a comparison of approximate dose levels (mg/kg) rather than dietary concentration (ppm) (Potrepka, 1978). Use of either figure would result in a margin of safety within the same order of magnitude.

If the assumption is made that the subacute model is more analogous to applicator exposure, no correction would be made for the time span of the exposure, and the applicable NOEL would be 500 ppm. Calculations based on this assumption would yield an estimated maximum dietary equivalent of 6.7 - 2.1 ppm. Using the subacute NOEL, 500 ppm, as a basis, the margin of safety would range from 43 -135.

III. Benefit Analysis[10/]

A. Introduction

This section summarizes the benefits of the principal uses of chlorobenzilate. The summary identifies the uses of the pesticide; estimates the quantities used; identifies and evaluates the registered alternatives, their availability and their costs; and evaluates the consequences of cancelling chlorobenzilate for these uses, including the projected impacts on crop production costs and retail food prices. This information is derived in part from rebuttal submissions.

B. Uses

For purposes of discussion, the uses of chlorobenzilate may be grouped into two categories, citrus and non-citrus uses. Table 1 presents the complete usage pattern for chlorobenzilate in the United States.

1. Citrus Uses

The most extensive use of chlorobenzilate is to control mites on citrus crops, principally oranges, grapefruit, and lemons. The major target pests are the citrus rust mite on oranges and grapefruit and the citrus bud mite on lemons. In 1975, chlorobenzilate use on these three crops accounted for approximately 920,000 pounds of active ingredient; other citrus uses (limes, tangelos, tangerines, other specialty citrus

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10/ This section is based on analyses prepared by M. Luttner and M. McWhorter, Criteria and Evaluation Division, OPP, EPA. All references are from Luttner unless otherwise noted.

fruit) accounted for 76,000 pounds. In total, citrus uses accounted for 89.2% of all chlorobenzilate used in the United States.

About 50% of U.S. citrus acreage, over 620,000 acres and 11,400 farms, is treated with chlorobenzilate. Florida citrus growers use chlorobenzilate most extensively. Two-thirds (523,000 acres) of the Florida acreage used to grow oranges, grapefruit, and lemons is treated with chlorobenzilate, accounting for 72% of the total chlorobenzilate used in the United States. Approximately half (43,000 acres) of the Texas acreage is treated with chlorobenzilate, which accounts for 9% of the total chlorobenzilate used in the United States. Only 1.6% of the California citrus acreage is treated with chlorobenzilate, which accounts for under 1% of the total chlorobenzilate used in the United States. Another 7% of chlorobenzilate used in the United States is applied to limes, tangerines, tangelos, and other specialty citrus crops.

a. Florida

In Florida, chlorobenzilate plays an integral part in established citrus integrated pest management programs. At present these programs are directed at controlling the principal pests of Florida citrus, the citrus rust mite and the citrus snow scale (Brogdon, 1976). Chlorobenzilate is recommended for use in these programs because it controls citrus rust mites without harming the natural predators and parasites of the scale insects and because it is cost-effective. Florida citrus IPM programs have reduced previously important pests, such as purple scale and Florida red scale, to relative insignificance through the introduction and establishment of parasites on virtually all of the Florida citrus acreage.

Through the IPM program, another parasite, the Hong Kong wasp, is being introduced to control snow scale.

b. Texas

The principal pest in Texas citrus production is the citrus rust mite (French et al., 1978). As in Florida, chlorobenzilate is effective in controlling the citrus rust mite while preserving beneficial insects important in the control of chaff, California red, Florida red, purple, and brown soft scales. Seventeen species of beneficial insects were released in Texas citrus production areas during the period 1952-1960 (Cocke et al. 1978); as a result, beneficial insects have provided significant control of purple and Florida red scale (Dean, 1955, 1975).

The citrus mealybug is also regarded as a potentially major pest that is currently being controlled in Texas by species of lady beetles and brown lacewing. Field experimentation indicates that the lady beetle can effectively control citrus mealybug in orchards treated with chlorobenzilate.

Extension education programs backed by citrus IPM research at the Texas Agricultural Experiment Station, Texas A&I University, and the USDA-Subtropical Texas Area Citrus Insects Laboratory are helping Texas growers to become aware of and to adopt citrus IPM control strategy. Because of the growing acceptance of IPM, a Texas Citrus Pest Management Program that will include insect, mite, and disease control is being developed (Cocke et al. 1978).11/

11/ Citrus IPM in Texas is currently on a less formal basis than citrus IPM is in Florida. However, beneficial insects established through releases provide biological control of scale pests. In Texas as in Florida, the use of selective miticides like chlorobenzilate protects these beneficial insects, requiring less use of broad-spectrum scalicides than would otherwise be required.

c. California

In California, chlorobenzilate is used on an "as needed" basis (alone and in combination with oil) to control citrus bud mite on lemons and citrus rust mite on oranges. About one eighth (approximately 5,000 acres) of the lemon acreage in the southern counties[12] is treated with chlorobenzilate in any given year; approximately one tenth (3,300 acres) of the orange acreage in the same area is treated annually (USDA, 1977). Integrated pest management programs in the southern counties are used to varying degrees for control of California red, purple, and black scales, and brown soft scales, aphids, and mealybugs. Chlorobenzilate is used in these programs because it is compatible with the use of the *Aphytis* parasites to control California red scale, and has no adverse effect on the natural predators of mites and other pests (Jeppson, 1959).

d. Arizona

Three major mite problems occur annually on citrus crops grown in Arizona - citrus red mite, citrus flat mite and Yuma spider mite. A fourth species, the Texas citrus mite, is an occasional problem in local areas (Luttner, 1977a). The citrus red mite is principally a pest specific to lemons in Arizona, while the other mite species affect all of the citrus crops. Chlorobenzilate is used by Arizona growers for the same reasons it is used elsewhere, i.e., its selectivity for mites and negligible effects upon beneficial insects. Approximately 5% (3,000 acres) of the

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[12] The southern California counties in question include the following: Imperial, Los Angeles, Orange, Riverside, San Diego, Santa Barbara, and Ventura.

Arizona acreage used to grow oranges, lemons, and grapefruit (principally lemons) is treated with chlorobenzilate (Table 1).

2. Non-Citrus Uses

Cotton use accounts for 39,000 pounds or 5% of the total chlorobenzilate used in the United States (1975). This amount was used on 39,000 acres of cotton or 0.41% of the total U.S. cotton acreage. Non-citrus fruits and nuts (apples, pears, cherries, almonds, and walnuts) account for 81,000 pounds or 7.3% of the total chlorobenzilate used in the United States (1975). This amount was used on 24,000 acres of fruits and nuts or approximately 1% of the total U.S. fruit and nut acreage.

There are other registered uses of chlorobenzilate, including melons, ornamentals, boats, and docks.[13] Little chlorobenzilate is applied for these uses (USDA, 1977).

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[13] The registered miticide uses of chlorobenzilate other than the citrus use, the cotton use, and the uses on fruits and nuts are:

agricultural crops	- melons (casaba, cantaloupes, crenshaw, honeydew, Persian);
ornamentals	- (lawns and turf) - grass;
	- (herbaceous plants and bulbs) - aster, carnations, chrysanthemums, gladioli, iris, marigold, phlox, snapdragon, zinnia;
	- (woody shrubs, trees and vines) - arbovitae, azaleas, birch, boxwood, camellia, Douglas fir, elm, hawthorn, hemlock, holly, juniper, lilac, locust, maple, oak, ornamental shrubs, ornamental trees, pine, poplar, rhododendron, roses, spruce, willow yew;
domestic dwellings; medical facilities & schools; commercial establishments	- (areas other than edible-product areas) - outdoor areas, boats,and docks.

Source: EPA Compendium of Registered Pesticides (U.S. Environmental Protection Agency, 1973).

C. Alternatives to Chlorobenzilate

1. Citrus Alternatives

If chlorobenzilate were not available for use as a miticide, citrus growers would face a choice of using no miticides or using miticide alternatives to chlorobenzilate. If growers in Florida, Texas, and Arizona decided to use an alternative miticide, they would face the decision whether to use one of the two selective alternatives or one of the non-selective alternatives. California growers would not have the option of choosing a selective alternative.

a. No Miticide

Uncontrolled, mites affect fruit size, appearance, crop yield, and tree stock stamina (Table 9). Fruit size and appearance are important for the fresh-fruit market because of consumer preference. Approximately 57% of the citrus fruit grown in Texas goes to the fresh fruit market. In California, 52% of the lemons and 65% of the oranges go to the fresh market.[14/] While only 5% of the Florida citrus crop goes to the fresh fruit market, growers cannot identify the fruit which goes to that market until the end of the season. Since the fresh fruit market is more lucrative than the process market, growers try to produce for this market by protecting the appearance of their fruit.

Studies have shown (Allen, 1978) that uncontrolled mites cause reductions in fruit size of 12% for oranges and 17% for grapefruit. Fruit-size declines also occur in lemons, but these effects have not been fully

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14/ State-wide average (Luttner, 1978a).

Table 9

ESTIMATE OF THE MAXIMUM ECONOMIC VALUE LOST AS A RESULT OF UNCONTROLLED MITE INFESTATIONS IN CITRUS [1]

State [2]	Crop	Average Production (tons) [3]	Loss Due To Drop (tons)	Loss Due To Size Reduction (tons)	Total Loss (tons)	Value [3] ($/ton)	Total Value of Production Loss
CA	lemons	735,000	183,750	—	183,750	116	$ 21,315,000
FL	oranges	8,119,000	811,900	906,080	1,717,980	58	$ 99,643,000
	g-fruit	2,057,000	205,700	314,721	520,421	57	$ 29,664,000
							$129,307,000
TX	oranges	248,000	24,800	27,677	52,477	52	$ 2,729,000
	g-fruit	405,000	40,500	61,965	102,465	51	$ 5,226,000
							$ 7,955,000
Total Per Year							$158,577,000

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[1] Luttner, (1978a)

[2] No estimate of impact could be derived for Arizona

[3] 3-Year average based on USDA statistics

quantified. Also, overall yield can be reduced by mite infestations due to fruit drop (Allen, 1978). It is estimated that such reductions in fruit size and overall yield would reduce grower gross revenues by about $159 million per year (Table 9). Total grower gross revenues from sales of citrus crops approximate $1 billion per year. Finally, failure to control mites reduces the life span of citrus trees, causing further economic impacts.

b. Alternative Miticides: Florida and Texas

Chlorobenzilate is used widely because its selectivity makes it compatible with integrated pest management programs using predators and parasites of pests other than mites, principally scale insects. Such IPM programs provide inexpensive control of a number of major pests. Accordingly, assessment of pesticide alternatives to chlorobenzilate must focus on the economic consequences of replacing chlorobenzilate with a selective miticide, compatible with these integrated pest management programs, or with a non-selective miticide, which would disrupt those programs.

i. Selective Miticides

Only two registered selective miticides[15/] are potential chlorobenzilate alternatives in Florida and Texas: dicofol and fenbutatin-oxide.[16/]

[15/] Several pesticides unregistered for citrus uses may be useful as chlorobenzilate alternatives. Diflubenzuran (under pre-RPAR review by the Agency) has performed adequately in pre-development testing. Hirsutella, a naturally-occurring fungal disease of mites, has shown effectiveness under some conditions (McWhorter, 1978). The Agency is not evaluating unregistered potential alternatives in this document.

[16/] The Agency has conducted a preliminary risk assessment of dicofol and fenbutatin-oxide (see Appendix C). In broad summary, dicofol appears to be an oncogen based upon preliminary results of an NCI study, while fenbutatin-oxide appears to cause reproductive effects and may pose other problems.

Both pesticides are included in the respective State recommendations for mite control (Luttner, 1977a, 1978b). However, each poses substantial problems as an acceptable substitute in IPM programs.

Total per-acre treatment costs with dicofol are approximately 33% higher than total per-acre treatment costs with chlorobenzilate (Table 10). If dicofol is used in groves infested with snow scale (approximately 75% of Florida groves), the snow scale populations increase, causing serious infestation and necessitating the use of scalicides (Florida Cooperative Extension Service, 1977).[17/]

Growers using dicofol in place of chlorobenzilate in groves infested with snow scale would need to supplement dicofol applications with scalicide applications. However, since snow scale is not a citrus pest in Texas, it is unlikely that scale problems in Texas would be aggravated by the use of dicofol. The per-acre cost of treatment with dicofol is approximately $32.67, compared to $24.62 per-acre using chlorobenzilate.

Fenbutatin-oxide (marketed under the trade name Vendex) is a selective miticide which does not cause proliferation of snow scale or other pests (Cocke et al. 1978). However, fenbutatin-oxide is expensive in comparison with chlorobenzilate and other alternative miticides. In Florida, the per-acre cost of treatment with fenbutatin-oxide ranges from $63.31 to

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[17/] The observed field sex ratio of snow scale is normally 5 males to 1 female. Applications of dicofol have increased average populations approximately three-fold. Additionally, the sex ratio of the F_1 progeny is approximately 3 females to 1 male, thus greatly expanding the population's potential for increase (Brooks, 1973; Huffaker, 1978).

Table 10

PER-ACRE TREATMENT COSTS IN FLORIDA CITRUS WITH CHLOROBENZILATE; SELECTED ALTERNATIVE MITICIDES AND SCALICIDES[1]

Target Pests	Pesticide	Cost ($)[2]	Material[3] Cost/Acre ($)	Total Cost/Acre[4] Treatment ($)
Mites	Chlorobenzilate 4E	16.00/gal	5.00	24.62
	Dicofol 4MF	17.40/gal	13.05	32.67
	Ethion 4E	13.50/gal	12.66	32.28
	Sulfur 95%	120.00/ton	3.00	22.62
	Ethion 4E & Oil 97%	13.50/gal + $1/gal	12.66 + 6.00 = 18.66	38.28
	Oil 97%	1.00/gal	8.00	27.62
	Fenbutatin-Oxide 50WP	11.65/lb	43.69	63.31[5]
Scales	Ethion 4E	13.50/gal	12.66	32.28
	Parathion 8E	16.00/gal	5.00	24.62
	Carbophenothion 4E	13.50/gal	12.66	32.28
	Oil 97%	1.00/gal	10.00	29.62

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[1] Selected on basis of use or potential for use.

[2] Material costs as reported for Florida by the USDA Chlorobenzilate Assessment Team.

[3] Material costs per acre based on Florida costs and application rates specified in the Florida Citrus Spray and Dust Schedule.

[4] Total costs include application costs per acre of $19.62, which represents typical Florida costs for a dilute (1,000 gallons spray/acre) spray treatment with tractor-pulled air-blast equipment.

[5] The total cost/acre treatment would increase to $69.87 if 6 pints of a surfactant were added per acre.

$69.87 (depending upon whether a surfactant is added);[18] in Texas, the per-acre cost of treatment with fenbutatin-oxide ranges from $40.01 to $46.57. The per-acre cost of treatment with chlorobenzilate is $24.62 (Table 10).

Another problem associated with the use of fenbutatin-oxide in Florida (but not Texas) is its incompatibility with oil. Fenbutatin-oxide and oil are phytotoxic when applied together or within 30 days of one another.[19] Oil is the treatment of choice for greasy spot, a fungal disease which is one of the major pest problems of Florida citrus.[20] Mite problems and greasy spot problems frequently occur at the same time. If it is possible to delay treatment of these pests for 30 days, then fenbutatin-oxide and oil can both be used for control of greasy spot disease and mites; however, the use of fenbutatin-oxide in the spray program would increase grower costs, since two separate treatments would be required in place of a single chlorobenzilate plus oil treatment. This increase would amount to the $19.62 per-acre application cost. It is frequently not prudent, however, to defer treatment of greasy spot or mites for 30 days. In such situations, fenbutatin-oxide could only be used if some other pesticide could be substituted for oil to control greasy spot disease. If benomyl[21/] were substituted for oil, the additional cost to growers would be $8.00, the difference between the material cost of benomyl and the material cost of oil.

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[18] Because fenbutatin-oxide does not act as rapidly as chlorobenzilate, the use of fenbutatin-oxide may require the addition of a surfactant to produce results equivalent to those obtained with chlorobenzilate.

[19] The phytotoxicity problem occurs primarily with immature fruit and foliage. However, since all trees in a grove may contain both mature and immature fruit and/or foliage at any one time, phytotoxicity is appropriately treated as a generic problem.

[20] Other pesticides registered and recommended by the State of Florida for control of greasy spot disease are: difolatan, benomyl, copper, oil.

Further, while fenbutatin-oxide can substitute for chlorobenzilate on oranges and most grapefruit varieties, it is not registered for the remaining chlorobenzilate citrus uses.[22/] Fenbutatin-oxide has not been used widely in the past, and it may not be immediately available in sufficient quantity to be used as a substitute for chlorobenzilate. There is no reason to believe, however, that the supply of fenbutatin-oxide would not increase to meet demand if that demand were created by cancellation of chlorobenzilate.

ii. Non-Selective Miticides[23/]

Certain of the non-selective alternatives to chlorobenzilate — ethion and ethion plus oil — can control mites as effectively as chlorobenzilate. Another non-selective alternative, sulfur, does not provide the level of mite control achieved with chlorobenzilate. Were these alternatives repeatedly used in place of chlorobenzilate,[24/] the populations of

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[21/] Currently under RPAR review.

[22/] Fenbutatin-oxide is currently registered for all citrus fruit except tangerines, tangelos, Reed grapefruit, or Webb Red Blush grapefruit (Luttner, 1978b).

[23/] The non-selective miticides for citrus mite control are carbophenothion, ethion, propargite, sulfur, ethion plus oil, carbophenothion plus oil, ethion plus sulfur, oil, dicofol plus oil. Only those materials judged to be major chlorobenzilate alternatives were evaluated for their impact upon beneficial insects (USDA, 1977).

[24/] Non-selective miticides are currently in use; however, the level of use is compatible with maintenance of beneficial insect populations.

the predators and parasites of the scale insects and other pests would be reduced to levels incapable of providing economic control, necessitating the use of combinations of chemical pesticides in large volumes (Table 11 and 12). In Florida, for example, the impact on existing IPM programs would be severe, and it is expected that at the end of the fifth year after cancellation of chlorobenzilate, growers using a non-selective alternative would need to treat 100% of their acreage with one application of a miticide and two applications of a scalicide (Table 11). The per-acre cost of such treatment would range from $72.00 to $103.00.[25/] A similar impact could be experienced by Texas citrus growers, many of whom are using pest management techniques similar to those used in Florida.

The use of non-selective chlorobenzilate alternatives and widespread scalicide treatments in Florida may have adverse effects upon fruit yield or grade and tree vitality. Adverse fruit quality effects may also occur in Texas (over one-half of all citrus produced in Texas is utilized in the fresh market). However, no valid estimates on the amount of fruit that would be damaged or unusable or the extent of tree injury are available to evaluate this potential impact.

c. Alternative Miticides: California

There is only one chlorobenzilate alternative (oil) for control of the citrus bud mite on the southern California lemon crop. Further, only one chlorobenzilate alternative (wettable sulfur) is recommended by the State of California for control of the citrus rust mite on southern

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[25/] The cost range is based on the following spray regimes: sulfur, parathion, parathion ($72.00) and ethion plus oil, ethion, ethion ($103.00).

Table 11

ESTIMATED EXTENT OF USE OF CHLOROBENZILATE AND SELECTED SUBSTITUTES TO REPLACE CHLOROBENZILATE FOR CONTROL OF THE CITRUS MITE COMPLEX AND SCALE INSECTS IN FLORIDA[1/]

	Miticide Use		Scalicide Uses		Total Use	
	Year 1	Year 5	Year 1	Year 5	Year 1	Year 5
Chlorobenzilate	805,000	805,000	—	—	805,000	805,000
Fenbutatin-Oxide[2/]	2,415,000	2,415,000	—	—	2,415,000	2,415,000
Dicofol	418,000	418,000	—	—	418,000	418,000
Ethion	979,000	979,000	319,000	1,594,000	1,298,000	2,573,000
Carbophenothion	—	—	319,000	1,594,000	319,000	1,594,000
Parathion	—	—	213,000	1,063,000	213,000	1,063,000
Sulfur	7,834,000	7,834,000	—	—	7,834,000	7,834,000
Oil (gals.)	1,949,000	1,949,000	850,000	4,250,000	2,799,000	6,199,000

[1/] Note that all of the listed materials (except fenbutatin-oxide) would have to be used in the quantities indicated to replace chlorobenzilate.

[2/] Quantity indicates potential use level (see discussion at Section III,C,b,i). Fenbutatin-oxide poses oil compatibility problems (see discussion at Section III,C,b,ii). In addition, there are problems concerning the availability of fenbutatin-oxide in the event of cancellation of chlorobenzilate (see discussion at Section III,C,b,i). Finally, fenbutatin-oxide is not registered for some Texas citrus uses (see discussion at Section III, C,b,i).

Table 12

ESTIMATED EXTENT OF USE OF CHLOROBENZILATE AND SELECTED SUBSTITUTES TO REPLACE CHLOROBENZILATE FOR CONTROL OF THE CITRUS MITE COMPLEX IN TEXAS[1]

	Quantity Required	
	Year 1	Year 5
Chlorobenzilate	102,000	102,000
Fenbutatin-Oxide[2]	51,000	51,000
Dicofol	174,000	174,000
cofol	31,000	31,000
Ethion	79,000	79,000
Carbophenothion	39,000	39,000
Oil (gals.)	199,000	199,000

1/ Note that all of the listed materials (except fenbutatin-oxide) would have to be used in the quantities indicated to replace chlorobenzilate.

2/ Quantity indicates potential use level (see discussion at Section III,C,b,i). There are problems concerning the availability of fenbutatin-oxide in the event of cancellation of chlorobenzilate (see discussion at Section III,C,b,i). Finally, fenbutatin-oxide is not registered for some Texas citrus uses (see discussion at Section III, C,b,i).

Table 13

ESTIMATED EXTENT OF USE OF CHLOROBENZILATE COMPARED WITH AMOUNT OF OIL TREATMENT TO REPLACE CHLOROBENZILATE FOR CONTROL OF THE CITRUS BUD MITE ON CALIFORNIA LEMONS

	Quantity Required	
	Year 1	Year 5
Chlorobenzilate	7,500	7,500
Oil (gals.)	493,000	2,465,000

California oranges (USDA, 1977).[26] Oil and sulfur are not completely satisfactory substitutes for chlorobenzilate since they are not as effective and their use damages fruit quality and tree vitality. However, the use of sulfur has an adverse effect on soil chemistry requiring compensating soil treatments with lime. The per-acre treatment cost of oil and sulfur would be approximately $76.00 and $23.00, respectively, compared with $61.00 for chlorobenzilate (USDA, 1977).

d. Alternative Miticides: Arizona

Although chlorobenzilate use is quite limited in Arizona citrus groves, the adoption of non-selective alternatives on those acres where chlorobenzilate is currently used would adversely effect the endemic parasite and predator populations in a manner similar to that described for Florida and Texas.

2. Non-Citrus Use Alternatives

There are numerous alternative pesticides registered to control mites on cotton and on fruits and nuts (Table 14). Should chlorobenzilate be cancelled as a cotton miticide, 10 of the 14 State-recommended alternatives would have a lower pesticide cost per acre. Even if efficacious control of the cotton spider mite could only be achieved with alternatives more expensive than chlorobenzilate, the increased pesticide cost to control mites on domestic cotton would be minimal - at most approximately $125,000 per year. Under a similar "worst case" assumption, the increased

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[26] Registered alternative treatments in use in Florida and Texas have been evaluated in California, but because of phytotoxicity problems, comparitive ineffectiveness, or other considerations, they have not been included for grower use.

Table 14

CHLOROBENZILATE AND ALTERNATIVES FOR NON-CITRUS USES

Commodity	Pesticide	Pesticide Cost/Acre ($)
Cotton		
	Chlorobenzilate	5.45
	Aldicarb	12.64
	Carbophenothion	2.20
	Demeton	3.80
	Dicofol	5.99
	Dicrotophos	0.71
	Disulfoton	2.40
	Ethion	3.44
	Methidathion	10.00
	Methyl Parathion	0.99
	Monocrotophos	3.16
	Parathion	1.12
	Phorate	4.20
	Propargite	6.04
	Sulfur	5.25
Walnuts		
	Chlorobenzilate	8.18
	Carbophenothion	7.00
	Dicofol	6.22
	Dioxathion	9.76
	Ethion	11.68
	Oil	7.75
	Phosalone	14.22
	Propargite	8.68
Apples		
	Chlorobenzilate	2.04
	Carbophenothion	3.50
	Cyhexatin	3.00
	Dicofol	2.92
	Ethion	1.46
	Propargite	2.17
	Tetradifon	1.77

U.S. pesticide cost to control mites on fruits and nuts would also be minimal - at most approximately $69,000 per year.

D. Grower Impacts

1. Citrus Uses

a. Florida

The economic impacts on growers associated with use of selected chlorobenzilate alternatives are elaborated in Tables 11, 16, and 19. Based upon the information previously presented, it has been determined that the non-selective chlorobenzilate alternatives[27/] would be the predominant replacement materials if chlorobenzilate were no longer available.

It was also previously explained that the use of dicofol for mite control would not have an adverse effect upon the beneficial insects that control purple and Florida red scale but would require additional use of scalicides to control increased populations of snow scale.

In the short run, fenbutatin-oxide is more expensive ($63.31/acre) than the chlorobenzilate miticide alternatives ($22.62 to $38.28 per acre). However, in the long run, the use of chlorobenzilate alternatives and scalicides would lead to per-acre costs ranging from $72 to $103. Thus, in strictly economic terms, fenbutatin-oxide would appear to be an attractive

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[27/] While non-selective materials would predominate, the economic assessment of the likely consequences of chlorobenzilate cancellation performed by the Agency (Luttner, 1977b) assumed that materials identified as likely replacements by the USDA Assessment Team would be used in equal distribution. In the case of Florida, one such material was dicofol, which is evaluated separately in this discussion from the standpoint of its suitability as a total chlorobenzilate replacement. Similarly, in the case of Texas, the analysis assumed that fenbutatin-oxide would be utilized to some extent.

Table 15

Impacts Projected to Growers Resulting from Cancellation of Chlorobenzilate 1/

Site 2/	Present Value of Change in Control Cost ($000) 3/	Affected Acres	Present Value of Change in Control Cost/ Affected Acre	Current Pest Control Cost/Acre 4/	% Change in Current Pest Control Cost/Acre	Current Production Cost/Acre 5/	% Change in Current Production Cost/Acre
FL-citrus	40,079	850,000	$47	$108	+43.5	$346	+13.6
CA-lemons	3,678	41,000	$90	$220	+40.9	$1,264	+7.1

1/ Source: Luttner, 1977a. Assumes non-selective alternatives are used to replace chlorobenzilate.

2/ Comparative data for Florida citrus is based on oranges, which comprise approximately 75% of the Florida acreage.

3/ Cost data represents fifth-year impacts calculated to present values using a 7% rate of discount.

4/ Represents an average for Florida oranges and California lemons, including pest, disease, and weed control. Based on budgets developed by Muraro and Abbitt (Florida) and Gustafson and Rock (California).

5/ Represents averages for Florida oranges and California lemons using budgets cited in footnote #3. Includes cultural costs and management only.

Table 16

Projected Cost of Scale Insect Control in Florida Citrus During Initial Five Year Period Following Cancellation of Chlorobenzilate

Scalicide 1/	Scalicide + Application Cost/Acre-Treatment($) 2/	Acre-Treatments/Year 3/				
		Year 1	Year 2	Year 3	Year 4	Year 5
Carbophenothion	32.28	85,000	170,000	255,000	340,000	425,000
Ethion	32.28	85,000	170,000	255,000	340,000	425,000
Oil (97%)	29.62	85,000	170,000	255,000	340,000	425,000
Parathion 8E	24.62	85,000	170,000	255,000	340,000	425,000
Totals	—	340,000	680,000	1,020,000	1,360,000	1,700,000

Scalicide 1/	Cost of Control/Year ($000) 4/				
	Year 1	Year 2	Year 3	Year 4	Year 5
Carbophenothion	2,744	5,488	8,231	10,975	13,719
Ethion	2,744	5,488	8,231	10,975	13,719
Oil (97%)	2,518	5,035	7,553	10,071	12,589
Parathion 8E	2,093	4,185	6,278	8,371	10,464
Totals	10,099	20,196	30,293	40,392	50,491

1/ The scalicides listed appear in the 1977 Florida Citrus Spray and Dust Schedule. The assumption that these materials would be widely used for scale control appears to be reasonable based on existing registrations, effectiveness, and low cost relative to other available scalicides.

2/ Costs based on the following: application rates as specified in the 1977 Florida Spray and Dust Schedule; pesticide prices supplied by the Assessment Team; application cost of $19.62 per acre represents use of dilute spray (two 500 gallon tanks/acre) as developed in a current production budget for Florida (Muraro and Abbitt, 1977 cited in Luttner, 1977b).

3/ Additional scale control treatments are assumed to be required on 100% of the Florida acreage (approx. 850,000 acres) over a five year period. The annual incremental increase in acres requiring treatment is assumed to be equal. The rate of increase in affected acres represents the projected rate of spread of economically damaging scale populations throughout the State. Use of scalicides on an equal basis represents an assumption by the analyst. Although chlorobenzilate is not used on 100% of Florida citrus each year, the projected IPM impacts will involve all of the State's acreage. Chlorobenzilate's use pattern (67% of Florida acreage treated/year) indicates that it is used two out of every three years on the average acre for mite control, with the numerous alternatives used in rotation during the third year. This occasional rotation with alternatives (some of which do not cause serious adverse effects upon beneficial insects) permits the continued success of the IPM program. However, continuous use of the alternatives would eventually lead to development of scale control problems on all of the Florida acreage.

4/ Product of scalicide + application cost/acre-treatment times acre-treatments for the respective years.

alternative. However, the profitability of the Florida citrus industry is highly variable and in many instances has been only marginally profitable or unprofitable as measured by return on investment (Brooke, 1973). Therefore, growers are likely to take a short-run view when selecting alternative pesticides, even though the most economical long run alternative would be a selective miticide.

Moreover, there are additional reasons why fenbutatin-oxide is unlikely to be adopted as an alternative to chlorobenzilate in Florida. These other reasons (both discussed earlier) are the oil incompatibility with fenbutatin-oxide and the fact that fenbutatin-oxide is not registered for some Florida citrus crops.

In Florida, using the non-selective regime to control rust mites would also require the use of two additional dilute scalicide treatments per year to counterbalance the reduction of currently established scale insect parasites to levels of population incapable of providing economic control. This phenomenon would occur on 100% of the commercial Florida citrus acreage over a five year period.

Using the non-selective regime would increase grower treatment costs by $2,043,000 per year or $3.17 per acre-treatment. The subsequent use of pesticides for scale insect control in Florida would increase grower costs by $50,491,000 in the fifth year after cancellation, i.e., when all of the Florida acreage would be receiving scale control treatments (Table 17). The costs could be expected to continue beyond the fifth year at the same relative level unless alternative scale control measures were developed.

Table 17

Economic Impact of the Loss of Chlorobenzilate During Initial Five Year Period Following Cancellation.

Year After Cancellation	Area	Cost of Mite Control with Alternatives ($000)[1]	Economic Cost of IPM impacts ($000)[2]	Present Value of Total Economic Impact ($000)[3]
1	AZ	0	0	0
	CA	658	—	658
	FL	2,043	10,099	12,142
	TX	274		274
	US	2,975	10,099	13,074
2	AZ	0	0	0
	CA	1,698	—	1,587
	FL	2,043	20,196	20,785
	TX	274		256
	US	4,015	20,196	22,628
3	AZ	0	0	0
	CA	2,739	—	2,392
	FL	2,043	30,293	28,242
	TX	274		239
	US	5,056	30,293	30,873
4	AZ	0	0	0
	CA	3,780	—	3,086
	FL	2,043	40,392	34,640
	TX	274		224
	US	6,097	40,392	37,950
5	AZ	0	0	0
	CA	4,821	—	3,678
	FL	2,043	50,491	40,079
	TX	274		209
	US	7,138	50,491	43,966

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[1] Costs for Arizona, Florida, and Texas derived in the Preliminary Benefit Analysis of Chlorobenzilate. Assumes that selected miticide alternatives (Luttner, 1977a; Tables 22, 23, and 24) would be utilized in an equal distribution on all acreage currently treated with chlorobenzilate. For a detailed discussion of the methodology utilized to derive the list of selected alternatives, (Luttner, 1977).

[2] Assumes 2 additional scale control treatments on 100% of Florida citrus acreage at year 5 and thereafter.

[2] Sum of cost of mite control with alternatives plus cost of IPM impacts; present values calculated using a 7 percent rate of discount.

The present value[28/] of this change in grower costs ($38,520,000) combined with the present value of the increased cost of chlorobenzilate alternatives for mite control in Florida ($1,559,000) is approximately $40,079,000 per year after five years. Given the annual cost of the current Florida citrus pest control program ($72.5 million), the impact ($40.08 million) projected to occur in the fifth year following a cancellation of chlorobenzilate would represent a 55.3% increase in the annual cost of the state's total citrus pest control program.

The loss of chlorobenzilate would increase pest control costs to Florida citrus growers by about $47 or 44% per acre after 5 years assuming widespread adoption of the non-selective regime. Average per-acre production costs for Florida citrus are projected to increase after 5 years by 13.6% (Table 15).

b. Texas

In Texas, the use of chlorobenzilate alternatives for control of citrus mites is projected to increase grower treatment costs by $274,000 per year or $4.72 per acre-treatment (Table 17).

Since snow scale is not a pest of major importance on Texas citrus, dicofol can be considered a satisfactory replacement for chlorobenzilate in existing pest management programs. If dicofol were the sole alternative used on those acres currently treated with chlorobenzilate, Texas citrus growers would incur additional mite control costs of approximately $432,000 per year or $7.32 per acre treatment.

[28/] "Present value" is an accounting concept used to represent future monetary impacts at a common point in time.

The per-acre cost of treatment with fenbutatin-oxide would increase from $24.62 to $40.01 (without surfactant) or to $46.57 (with surfactant). If all citrus acreage currently treated with chlorobenzilate were treated with fenbutatin-oxide, the total annual cost increase to growers would range from $908,000 (without surfactant) to $1,295,000 (with surfactant). Approximately 51,000 pounds of fenbutatin-oxide active ingredient would be required to replace the 101,500 pounds chlorobenzilate currently used in Texas citrus (Table 12).

c. California

In California, the use of petroleum oil sprays to control citrus bud mites on lemons would require one spray on all of the infested acreage and two sprays on two-thirds of the infested lemon acreage. This would occur over a five-year period on all of the lemon acreage in the southern counties. After five years, approximately 2,465,000 gallons of oil would be required to replace the 7,500 pounds chlorobenzilate active ingredient currently used on California lemons (Table 13).

In California the cost of controlling citrus bud mites on lemons is projected to increase pest control costs to growers by an additional $4,821,00 per year in the fifth year after cancellation (Table 17). This cost could also be expected to remain at the same level unless alternative citrus bud mite control measures were developed. The present value of the annual impact in the fifth year is approximately $3,678,000. Given an estimated cost of pest, disease, and weed control on lemons in the southern California counties of $9,020,000 per year, cancelling chlorobenzilate

zilate would increase the cost of pest control on the affected lemon acreage by about 40.8%.

The loss of chlorobenzilate would increase pest control costs for California lemon growers by about $90 or 41% per acre after 5 years. Average per acre production costs would increase after 5 years by about 7.1% (Table 15).

d. Arizona

The loss of chlorobenzilate and adoption of alternative miticides is projected to have no net cost to Arizona citrus growers. Using alternatives may disrupt IPM strategies in Arizona, but the extent of such disruption has not been identified nor the resulting costs quantified.

2. Non-Citrus Uses

The cost impacts to growers for non-citrus uses of chlorobenzilate are discussed in Section C,2.

E. Costs to the Citrus Pulp Feed Industry

Citrus pulp is a by-product of citrus processing; during the 1960's citrus pulp became a principal feed ration ingredient for dairy cattle in Florida. The majority (approximately 90%) of the domestic pulp feed market consists of sales to Florida dairymen with some sales to Florida beef ranchers. Approximately half of the 1,000,000 tons produced annually is exported to European markets where it is sold for use as dairy cattle feed. The use of citrus pulp as cattle feed produces gross revenues of approximately $70 to $90 million to the processors; however, due to the large amount of energy required to dry the pulp, net profits to the processors are not significant. However, the use of citrus pulp for cattle feed has solved a serious waste disposal problem for the citrus processors. Prior to the development of the citrus pulp-feed industry, the processing wastes were routinely dumped and left to rot in citrus groves. The utilization of pulp as an animal feed ingredient has thus turned a net cost segment of citrus processing into an outlet which provides some (though limited) net return to processors (Luttner, 1978g).

Since there is currently no alternative use for citrus pulp, a more costly disposal procedure (e.g., incineration or land-filling) would probably be necessary if citrus pulp were to be disallowed as cattle feed (Luttner, 1978g). Therefore, in order to protect the cattle feed ingredient business as an outlet for the by-products of citrus processing, the citrus processors would probably refuse to purchase chlorobenzilate-treated fruit if a restriction is enacted which prohibits chlorobenzilate residues in pulp. The residue restriction would result in a de facto cancellation of chlorobenzilate, leading to the citrus IPM impacts previously discussed.

F. Costs to Consumers

1. Citrus Uses

Consumers would be adversely affected due to higher prices and/or fruit quality considerations only if the loss of chlorobenzilate leads to significant reductions in yield and/or fruit grade. However, since yield and/or quality changes are not immediately projected to occur, there would be little change in the quantity of citrus supplied. Also, the citrus industry is relatively stable since growers cannot elect alternative land uses in the short run; therefore, a substantial supply response would not be expected in response to changes in cost. Because potential yield/quality effects are not indicated, and given the history of excess production in the domestic citrus industry (which leads to a relatively weak market position for growers)[29/] the projected costs would be absorbed by growers, at least in the short term, with little or no consumer impacts anticipated.

2. Non-Citrus Uses

The analysis indicates that the potential cancellation of chlorobenzilate for use on non-citrus crops would have insignificant effects upon growers, marketers, and consumers of these crops. The reasons are:

1) Only small quantities of chlorobenzilate are used to control mites on cotton and a wide variety of fruit and nut crops.
2) Numerous chlorobenzilate alternatives are both registered and recommended for use on cotton, fruits, nuts, and other crops.
3) Certain of the alternatives can be used at a lower pesticide cost per acre.

Should the cancellation of chlorobenzilate result in the use of higher-cost alternatives on non-citrus crops, the total estimated increase

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[29/] This phenomenon is reflected by citrus cold storage figures, which relect the large stocks of citrus products carried over from one year to the next (USDA, 1977).

in pesticide cost is $194,000 per year. Of this total, cotton accounts for $125,000; fruits, nuts, and other crops for approximately $69,000. If the total non-citrus production cost-increase were completely passed on to final domestic consumers under the assumption of no reduction in yields, the consumer impact would be minimal.

IV. Risk-Benefit Analysis of Alternative Courses of Action

Evaluation of the risk and benefit data suggests seven principal regulatory options:

A. Continue Registration of All Uses.

B. Cancel All Uses.

C. Continue Registration of Chlorobenzilate Use on Citrus and Amend the Terms and Conditions of Registration; Cancel All Other Uses.

D. Cancel Chlorobenzilate Use on Citrus To Take Effect After Five Years, and in the Interim Amend the Terms and Conditions of Registration; Cancel All Other Uses.

E. Continue Registration of Chlorobenzilate Use on Citrus, Amend the Terms and Conditions of Registration, Require That Identified Exposure Data Be Submitted to EPA in 18 Months; Reevaluate the Use on Citrus After Additional Exposure Data Becomes Available; Cancel All Other Uses.

F. Continue Registration of Chlorobenzilate Use on Citrus in Florida, Texas, and California, Amend the Terms and Conditions of Registration, Require that Identified Exposure Data be Submitted to EPA in 18 Months; Reevaluate the Use on Citrus After Additional Exposure Data Becomes Available; Cancel Use on Citrus in Arizona and All Other Uses.

G. Continue Registration of Chlorobenzilate Use on Citrus, Amend the Terms and Conditions of Registration; Prohibit the Use of Pulp from Chlorobenzilate-Treated Citrus as Cattle Feed; Establish Complementary Tolerances; Cancel All Other Uses.

Tables 18 and 19 summarize the risks and benefits of each option. The specific risks and benefits pertaining to each option are described below.

Table 18

REGULATORY OPTIONS AND MAXIMUM RISK INCIDENCE FROM CLOROBENZILATE USE

OPTION	FLORIDA CITRUS CONSUMERS	REMAINDER OF US CITRUS CONSUMER	CITRUS PESTICIDE APPLICATOR	FLORIDA CITRUS PICKERS	NON CITRUS USE CONSUMERS	NON-CITRUS PESTICIDE APPLICATION	NON-CITRUS US PICKERS
A. Continue Registration of All Uses	2.6 to 6.4 per million	2.0 per million	400 to 1400 per million	No Data	0.1 per million	No Data	No Data
B. Cancel All Uses	0	0	0	0	0	0	0
C. Continue Registration of Chlorobenzilate Uses on Citrus and Amend the Terms and Conditions for Registration; Cancel All Other Uses	2.6 to 6.4 per million	2.0 per million	4 to 278 per million	No Data	0	0	0
D. Cancel Chlorobenzilate Use on Citrus To Take Effect After 5 Years and in the Interim Amend the Terms and Conditions for Registration; Cancel All Other Uses	0.2 to 0.5 per million	0.1 per million	0.3 to 20 per million	Reduced Exposure	0	0	0
E. Continue Registration of Chlorobenzilate Use on Citrus Amend Terms and Conditions of Registration, Require that Identified Exposure Data be submitted to EPA in 18 Months; Reevaluate the Use on Citrus After Additional Exposure Data Becomes Available; Cancel All Other Uses	2.6 to 6.4[a] per million	2.0[a]	4 to 278[a] per million	No Data	0	0	0

(Table 18 Cont'd)

F.	Continue Registration of Chlorobenzilate Use on Citrus in Florida, Texas, and California; Amend Terms and Conditions of Registration, Require that Indentified Exposure Data be submitted to EPA in 18 Months; Reevaluate the Use on Citrus After Additional Exposure Data Becomes Available; Cancel Use on Citrus in Arizona and All Other Uses	2.6 to 6.4[a] per million	----marginal risk reductions for for consumers coincident with an approximate 3,000 acre reduction in use, applicator risk in Arizona eliminated---	No Data	0	0	0
G.	Continue Registration of Chlorobenzilate Use on Citrus; Amend the Terms and Conditions of Registration; Prohibit the Use of pulp from Chlorobenzilate-Treated Citrus As Cattle Feed; Initiate Action for EPA to Establish a Tolerance on Chlorobenzilate Residue in Citrus Pulp; Cancel All Other Uses	2[b] per million	2[b] per million	4 to 278[b] per million	No Data	0	0	0

[a] Additional data may result in regulatory action reducing rick below these estimates.

[b] Assumes that this approach will not create a _de facto_ cancellation; if the market forces a _de facto_ cancellation risks are 0 in every case.

Table 19

ECONOMIC IMPACTS RESULTING FROM CHLOROBENZILATE REGULATORY OPTIONS

Option	Commodity	Economic Impact [1]					
A. Continue Registration of All Uses	Citrus	None					
	Cotton	None					
	Fruits/Nuts	None					
B. Cancel All Uses	Citrus	Area	Economic Impact in Year After Cancellation ($000)				
		AZ	0	0	0	0	0
		CA	600	1,600	2,400	3,100	3,700
		FL	12,200	20,800	28,300	34,600	40,100
		TX	300	300	200	200	200
		US	13,000	22,600	30,900	37,900	44,000
		and thereafter [2] $4.4 to $19.1 million for amended use direction [3]					
	Cotton	$125,000/Yr					
	Fruit/Nuts	$69,000/Yr					
C. Continue Registration of Chlorobenzilate Use on Citrus and Amend the Terms and Conditions for Registration; Cancel All Other Uses	Citrus	$4.4 to $19.1 million for amended use direction [3]					
	Cotton	$125,000/Yr					
	Fruits/Nuts	$69,000/Yr					

(TABLE 19 Cont'd)

<table>
<tr><td>D.</td><td>Cancel Chlorobenzilate Use on Citrus to Take Effect After Five Years and in the Interim Amend the Terms and Conditions for Registration; Cancel All Other Uses</td><td>Citrus</td><td>No Impact Years 1-5
<table>
<tr><th>Area</th><th colspan="5">Economic Impact in Year Aftr Cancellation ($000)</th></tr>
<tr><td>AZ</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>CA</td><td>400</td><td>1,100</td><td>1,800</td><td>2,100</td><td>2,500</td></tr>
<tr><td>FL</td><td>8,700</td><td>14,800</td><td>20,000</td><td>24,600</td><td>28,500</td></tr>
<tr><td>TX</td><td>200</td><td>200</td><td>200</td><td>300</td><td>300</td></tr>
<tr><td>US</td><td>9,300</td><td>16,100</td><td>22,000</td><td>27,000</td><td>31,300</td></tr>
</table>
and thereafter 2/
$4.4 to $19.1 million for amended use direction 3/</td></tr>
<tr><td></td><td></td><td>Cotton
Fruits/Nuts</td><td>$125,000/Yr
$69,000/Yr</td></tr>
<tr><td>E.</td><td>Continue Registration of Chlorobenzilate Use on Citrus, Amend the Terms and Conditions for Registration, Require That Identified Exposure Data be submitted to EPA in 18 Months; Reevaluate the Use on Citrus After Additional Exposure Data Becomes Available; Cancel All Other Uses</td><td>Citrus</td><td>$4.4 to $19.1 million for amended use direction 3/
Potential for additional impacts dependent on test results</td></tr>
<tr><td></td><td></td><td>Cotton
Fruits/Nuts</td><td>$125,000/Yr
$69,000/Yr</td></tr>
<tr><td>F.</td><td>Continue Registration of Chlorobenzilate Use on Citrus in Florida, Texas, and California; Amend Terms and Conditions of Registration, Require that Indentified Exposure Data be submitted to EPA in 18 Months; Reevaluate the Use on Citrus After Additional Exposure Data Becomes Available; Cancel Use on Citrus in Arizona and All Other Uses</td><td>Citrus</td><td>$4.4 to 19.1 million for amended use direction 3/
Arizona - no economic impact Potential for addtional impacts dependent on test results</td></tr>
</table>

(TABLE 19 Cont'd)

	Cotton	$125,000/Yr				
	Fruits/Nuts	$ 69,000/Yr				
G. Continue Registration of Chlorobenzilate Use on Citrus, Amend the Terms and Conditions of Registration, Prohibit the Use of Pulp from Chlorobenzilate Treated Citrus as Cattle Feed; Initiate Action For EPA to Establish a Tolerance on Chlorobenzilate Residue in Citrus Pulp; Cancel All Other Uses	Citrus	Economic Impact in Year After Cancellation ($000)				
		0	0	0	0	0
		600	1,600	2,400	3,000	3,700
		12,200	20,800	28,300	36,600	40,000
		300	200	200	200	200
		13,000	22,600	30,900	38,000	44,000
		and thereafter 2/,4/				
		$4.4 to $19.1 million for amended use direction 3/				

1/ All future dollar impacts are given in present values. The citrus cancellation impact in year 1 ($13,000,000) is of the same magnitude as the first-year impact if it is delayed until the sixth year ($9,322,000). However, the discounting factor reduces present value of the sixth-year impact relative to the first-year impact.

2/ Assumes no establishment of viable substitute compatible with IPM and at cost approximately equivalent to chlorobenzilate's.

3/ Protective clothing costs for applicators was assumed to be negligible. (Respirators $15 each). Enclosed cab costs range from $4,250 (cab purchase) to $18,290 (new tractor with cab). Total $4.4 to $19.1 million 1,045 applicators depending on whether tractors are adapted or replaced would be the maximum potential capital outlay. These capital outlays are for air-conditioned cabs; the cost estimates do not reflect the use of positive-pressure air filtration systems.

4/ Assumes loss of feedstuff market will cause growers to cease using chlorobenzilate; if not then same impact as Option C.

A. Continue Registration of All Uses

Adopting option A would indicate the Agency's conclusion that the risks associated with each use are outweighed by the respective benefits and therefore, that none of the uses of chlorobenzilate cause unreasonable adverse effects. This option would return pesticide products which contain chlorobenzilate to the registration process for reregistration.

This option would not reduce the risk of cancer nor the risk of testicular effects associated with the use of chlorobenzilate. The potential lifetime risk of cancer from all uses would remain at 2.1 in one million for the U.S. population; at 2.7 to 6.5 in one million for the Florida population; and at 400 to 1400 in one million for ground applicators of chlorobenzilate (Table 18). The ground applicators' margin of safety from testicular effects would remain in the range from 43 to 169.

There would be no adverse economic impacts associated with this option. This option would retain the usefulness of chlorobenzilate as a cost-effective tool for control of the mite complex, as well as the existing benefits from its use in citrus integrated pest management programs.

The choice of this option would indicate the Agency's willingness to tolerate a level of risk greater than the levels of risk estimated for the other options (Table 18) because there are no adverse economic effects (Table 19) or loss of other benefits.

B. Cancel All Uses

Adopting option B would indicate the Agency's conclusion that the risks associated with each use outweigh the respective benefits and thereby result in unreasonable adverse effects. This option would eliminate all uses of chlorobenzilate.

Cancellation would eliminate all the risks associated with the use of chlorobenzilate (Table 18) but at great cost to citrus growers. These costs are based on the assumption that no alternative miticides as effective as chlorobenzilate nor as compatible with citrus integrated pest management programs would be developed and marketed at competitive cost. In the fifth year after the cancellation of chlorobenzilate, the citrus industry's additional pest management control costs would stabilize at $44 million per year. Florida growers would incur 90% of the increased cost generated by using chlorobenzilate substitutes (Table 19).

In addition, the switch to alternatives may involve undesired risk consequences. To obtain the degree of pest control currently obtained in citrus integrated pest management programs using chlorobenzilate, increased amounts of these substitute chemicals would be required (Table 9). At the present time, the safety data on several of these substitutes (carbophenothion, ethion, sulfur, and propargite) is incomplete.

The annual economic impacts of cancelling chlorobenzilate's non-citrus uses are relatively small, ranging from $69,000 on fruits and nuts to $125,000 on cotton.

The choice of this option would indicate the Agency's unwillingness to tolerate the level of risk associated with all uses, based on a conclusion that the benefits do not outweigh those risks (Tables 18 and 19).

C. Continue Registration of Chlorobenzilate Use on Citrus and Amend the Terms and Conditions of Registration; Cancel All Other Uses

Option C would indicate the Agency's conclusion that the benefits arising from the use of chlorobenzilate on citrus in Florida, Texas, California, and Arizona exceed the risks (reduced by amending the terms and conditions of registration) estimated to exist from the use of chlorobenzilate on citrus in each of these four States. Option C would indicate, moreover, that the risks associated with the non-citrus uses of chlorobenzilate are not outweighed by these benefits.

1. Economic and Environmental Considerations

The economic and other impacts of cancellation of chlorobenzilate for use on Florida, Texas, Arizona, and California citrus are discussed in detail in Part III of this document.

In general, it is likely that cancellation of the uses of chlorobenzilate on citrus in Florida would result in extensive use of non-selective miticides - principally organophosphates - and consequent destruction of existing IPM programs. Per-acre treatment costs would increase sharply - from $24.62 to between $72 and $103 in the fifth year after cancellation and thereafter. The aggregate cost impact of the expected use of non-selective pesticides could range from $40.3 million to $66.6 million annually in the fifth year after cancellation and thereafter. In addition to imposing a severe cost impact, the use of non-selective organophosphates would involve a substantial increase in the volume of pesticides used which could cause undesired adverse effects, including adverse health impacts. Fenbutatin-oxide, a selective miticide compatible with IPM programs, could be used to some extent but fenbutatin-oxide would be unlikely to gain acceptance because of its high cost and inappropriateness in some situations.

In Texas, dicofol probably would gain increased usage, since its cost would be only 33% higher than chlorobenzilate's and it could be used in IPM programs. However, recent preliminary NCI data indicate that dicofol may pose a more serious risk of cancer than chlorobenzilate.[30] Fenbutatin-oxide could substitute for chlorobenzilate in many instances and would be compatible with IPM programs. Fenbutatin-oxide's per-acre treatment cost increase over chlorobenzilate is lower in Texas than in Florida, but treatment costs with fenbutatin-oxide would be twice as high as treatment with chlorobenzilate. Moreoever, fenbutatin-oxide may pose a more serious risk of reproductive effects than chlorobenzilate.[30] In Texas, as in Florida, growers may choose non-selective pesticides to replace chlorobenzilate; the IPM impacts of such a choice would be similar to those predicted for Florida. As for Florida, a conclusion that the benefits of the citrus uses of chlorobenzilate in Texas exceed the risks would be based upon both economic and health concerns but the health concerns would weigh more heavily and the economic concerns less heavily than for Florida.

In Arizona, the economic consequences of cancellation would be insignificant.

30/ See Appendix C.

In California, a conclusion that chlorobenzilate's citrus uses should be continued would reflect a determination that the risks are small when weighed against the absence of satisfactory alternatives for the control of the citrus bud mite and the citrus rust mite.

2. Proposed Restrictions

The data show that the populations at risk with respect to chlorobenzilate use are the U.S. population at large, Florida residents, pesticide applicators, and citrus pickers. Under this option, pesticide applicator exposure would be reduced by changes to the terms and conditions of registration. Directions for use would be modified so that citrus growers would be allowed to select one of the following application methods:[31]

i) Ground application with applicators using additional protective clothing and respirators.

ii) Ground application with applicators using suitably-equipped enclosed cabs.

iii) Aerial application

In addition, the following registration amendment would be required for the continued use of chlorobenzilate on citrus:

iv) Classify as a restricted use pesticide, for use by or under the direct supervision of certified applicators.

Based on data and experience from other pesticides, the Agency has concluded that the measures described below would reduce exposure to chlorobenzilate applicators and therefore would reduce a substantial portion of the risk from chlorobenzilate use.

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[31] See Appendix D for specific label amendments.

Protective clothing and respirators could reduce the ground applicators' exposure and potential risks. The exposure estimates for ground applicators (Severn, 1978) are based on exposure to arms, hands and face (15.8% of the total body surface); covering the arms and hands would reduce the dermal exposure from between 12-40 mg/day to between 2.4-8.0 mg/day. Therefore, to reduce the exposure the Agency would require applicators to wear heavy-duty work gloves and full-length, long-sleeved, one-piece jumpsuits made of fine weave fabric (jersey) (Griffiths, 1978). Both would have to be laundered after each day of use. Applicators would also be required to wear a broad-brimmed hat. Further, face-piece respirators would effectively eliminate exposure by inhalation, estimated at 1 mg/day without protection. Therefore, the Agency would require applicators to wear suitable respirators which fit over the mouth and nose and have a filtering cartridge (NIOSH approved respirators for pesticide spray applicators referred to in Appendix D).

Protective clothing and respirators would reduce citrus pesticide ground applicators' estimated lifetime cancer risk (Table 18) by a factor of five (Severn 1978). There would also be a greater margin of safety (215 to 845) from testicular effects. These risk reductions would outweigh the minimal cost for the protective clothing and the respirators.

Use of suitably-equipped enclosed cabs by applicators would also reduce ground applicator exposure and potential risks. The Agency would require that these cabs be completely enclosed and employ systems for delivering filtered air to the operator, as described in a recent study (Taschenberg and Bourke, 1975). In this study, the cab substantially reduced (99%) the amounts of pesticide spray which could come into contact with the applicator. Applying the results of this study to chlorobenzilate exposure estimates would reduce exposure from between 13 and 41 mg/day to between 0.13 and 0.41 mg/day when an enclosed cab is used. This would reduce the lifetime cancer risk to ground applicators from between 400 and 1400 to between 4 and 278 in one million. The margin of safety from testicular effects would be 4300 to 16,900. The costs of this approach cannot be fully assessed. However, the capital cost of air-conditioned cabs (which are anticipated to be somewhat less expensive than filtered air cabs) would run between $4.4 and $19.1 million if all growers selected this measure, depending upon the extent to which existing equipment could be retrofitted (Luttner, 1978). While growers have indicated interest in equipment of this type, it is probable that requiring enclosed cabs for all ground applicators would drive citrus growers to use other chemicals, rather than incur the capital cost of new application equipment.

Aerial application of pesticides is favored by some large growers, and current information indicates it would continue to be an accepted method of application where suitable. When chlorobenzilate is applied aerially, usually by helicopter, there is a minimum exposure to the applicator, but exposure from drift could potentially increase for people in the vicinity of citrus groves.

Classification to use only by certified applicators would also result in reductions in applicator exposure. The key concept behind classification to use by certified applicators is that certification can generally upgrade applicator skills and that with more skill and knowledge applicators are more likely to use pesticides carefully and efficiently. It would be reasonable to conclude that a general upgrading of the skills of chlorobenzilate applicators would, for these reasons, result in reduced exposures.

Cancelling the non-citrus uses of chlorobenzilate would have the impacts discussed in Option B.

Choice of this option would indicate acceptance of the level of risk to consumers from chlorobenzilate citrus uses and would reduce the level of risk (lowered by amended terms and conditions of registration) posed to applicators. However, this risk level is based on somewhat uncertain assumptions due to the lack of definitive data on exposure to chlorobenzilate. While the Agency would impose additional safeguards with regard to the level of risk posed to applicators, it has not recommended protective measures for citrus pickers because it has no data base upon which to evaluate risk to them.

D. Cancel Chlorobenzilate Use on Citrus to Take Effect After Five Years and In the Interim Amend the Terms and Conditions of Registration; Cancel All Other Uses.

Option D would indicate the Agency's unwillingness to accept the risk levels of Option C indefinitely, but would demonstrate acceptance of the Option C level of risk for a five-year period in order to reduce the initial economic impact and encourage technological innovation.

This option would reduce by approximately 14-fold the potential lifetime cancer risk and risk from testicular effects, since the period of exposure would be reduced from a lifetime to five years (Table 18). The combined effect of the amended use directions and the limited time span would reduce the risk of cancer for citrus pesticide applicators from 400 to 1400 per one million to between 0.3 and 20 per one million (Table 18). The testicular effects margin of safety for citrus pesticide applicators would be increased from between 43 and 169 to between 3,010 and 236,000.

This option would allow time to develop and register an alternative to chlorobenzilate (e.g. Zardex and Hirsutella) for use in citrus IPM programs. The five-year phase out would lessen the otherwise substantial impacts from the loss of chlorobenzilate.

Choice of this option would reflect a conclusion that the risks associated with the citrus uses are acceptable for the period of time necessary to develop and register an alternative compatible with IPM programs, in order to avoid the economic impacts of immediate cancellation (See Option B). However, choice of this option also would reflect a conclusion that indefinite, future use of chlorobenzilate involves risks which are unacceptable in view of the benefits, and that indefinite continued registration of chlorobenzilate creates unacceptable barriers to the development of alternatives.

This option would require the Agency to deal with two important areas of uncertainty: the period of time that would be necessary to develop and register an alternative(s), and the fact that the economic and environmental impacts of the alternatives which may be developed necessarily cannot be assessed at this time. Both areas of uncertainty would be addressed by the selection of a five-year phase out for chlorobenzilate. Generally speaking, 8 years are necessary to carry a pesticide all the way through the development and registration process, using the date that a compound is selected as a candidate for development in early screening tests. Since Zardex and Hirsutella are already well beyond this stage, a five year-period would seem adequate to accomplish development and registration of alternatives. Moreover, selection of a five-year phase out period would also reflect an Agency decision that sufficient time would be available after the registration (or failure to register) of an alternative(s) to permit applications for renewed registration of chlorobenzilate to be considered and acted upon.

Finally, it should be noted that selection of this option would reflect an Agency decision that incentives are necessary to stimulate development and registration of alternatives, and that the creation of incentives justifies the uncertainties and burdens associated with the options. Selection of this option would further reflect a decision that the probability that an alternative would be developed and registered is unacceptably low without the creation of incentives by the Agency.

E. Continue Registration of Chlorobenzilate Use on Citrus, Amend the Terms and Conditions of Registration, Require That Identified Exposure Data Be Submitted to EPA in 18 Months; Reevaluate the Use on Citrus After Additional Exposure Data Becomes Available; Cancel All Other Uses.

Option E would reflect an Agency conclusion that the risks of the non-citrus uses of chlorobenzilate outweigh the benefits and that the benefits of the citrus uses of chlorobenzilate outweigh the risks, as reduced by modifications to the terms and conditions of registration (see Option C). Option E would further reflect the Agency's conclusion that additional exposure data is necessary, and a determination to reevaluate the citrus uses of chlorobenzilate after these data are available.

This option would eliminate all risks associated with chlorobenzilate's non-citrus uses. It would require the same amended use directions as those explained in Option C for the continued use of chlorobenzilate products on citrus. It would also preserve the usefulness of chlorobenzilate in integrated pest management, at least until the additional data has been submitted to and evaluated by the Agency.

Option E would allow risks to continue at levels comparable to that of Option C but would require new data to substitute or refute current risk/benefit estimates or to indicate the need for a revised evaluation of risks and benefits. Should new data indicate higher risks or lower benefits than have been found in the present analysis, the Agency would reassess its regulatory decision. If the data confirms the present assessment, this option would be equivalent to Option C. The immediate economic impact of this option would be comparable to that of Option C.

If this option is adopted, registrants would be required to submit data derived from the studies described below; specific protocols have to be submitted by the registrants for approval within six months.

1. Citrus Fractionation Studies

Very little information is available on chlorobenzilate residues in citrus by-products. Limited data indicates that residues are present in citrus pulp and suggests the potential for residues in other by-products such as citrus oil. A fractionation study is necessary to measure chlorobenzilate residues in the by-products of citrus processing and, using these measurements, to estimate exposure from the products which have commercial utility. Since each residue analysis step (1 per by-product) is estimated to cost $100 to $200, and fractionation of citrus fruit requires approximately ten steps, the study would cost an estimated $1000 to $2000 for each citrus fruit type.

2. Feeding Citrus By-products to Cattle Study

Existing data indicates that chlorobenzilate residues are present in the citrus pulp used to feed cattle in Florida, and that milk and beef from cattle that were fed chlorobenzilate-contaminated pulp may contain chlorobenzilate residues. The proposed feeding study is needed to measure chlorobenzilate residues in milk and meat from cows that were fed pulp from citrus fruit treated with chlorobenzilate. Data from this study would be used to estimate exposure to Florida consumers from these dietary sources. The study would cost approximately $100,000.

3. Citrus Pickers Exposure and Re-entry Studies

The Agency has no data to determine whether chlorobenzilate residues on fruit surfaces and tree foliage create an exposure source to citrus pickers. Procedures which determine whether dislodgable chlorobenzilate residues adhere to pickers and the degradation rate of chlorobenzilate in field conditions will permit estimates of the occupational exposure and risk levels for pickers. These studies would cost between $100 and $200 per sample. Because sixty samples are estimated to be required, the total study would cost between $6,000 and $12,000.

4. Aerial Application Exposure Study

The Agency lacks data on exposure levels which result from the aerial application of chlorobenzilate. This study wwould provide relevant data concerning exposure to the drift which results from aerial application of pesticides in order to estimate chlorobenzilate exposure levels and evaluate the risk to nearby inhabitants.

The Agency estimates that the number of samples required may range from 500-1000 and at $100-$200 per sample, the study would cost between $50,000-$200,000.

5. Ground Applicator Exposure Study

The current exposure estimates for citrus ground applicators are based on studies with other pesticide sprays. An exposure study of chlorobenizilate ground applicators would allow better analysis and consequently better assessment of their potential risk from spray applications of chlorobenzilate. The study should cover mixing, loading and application exposure. The Agency estimates that 50 samples would be required at a cost of between $100 and $200 per sample; the entire study would cost $5,000-$10,000.

6. Residue Monitoring of Milk from Pulp-Fed Cattle and Residue Monitoring of By-products of Citrus Processing

While a preliminary analysis of milk samples from Florida does not indicate detectable residues of chlorobenzilate (Kutz, 1978), an earlier study (Formica et al., 1975) demonstrated chlorobenzilate residues in milk from cattle that were fed pulp to which chlorobenzilate had been added. In addition, there are studies by Mattson and Insler (cited in Severn, 1978) which indicate that chlorobenzilate residues could be expected to occur in beef. Therefore, a need exists to establish methods for detecting chlorobenzilate residues in milk and beef from cattle that have been fed pulp from chlorobenzilate-treated citrus fruit.

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Refinement of the analytical detection method is estimated to cost approximately $55,000. This assumes a 10% overhead cost. The estimated cost of monitoring the samples would be $100-200 per sample or an estimated $3,000-$6,000 for the entire sample monitoring study.

F. Continue Registration of Chlorobenzilate Use on Citrus in Florida, Texas, and California, Amend the Terms and Conditions of Registration, Require that Identified Exposure Data be Submitted to EPA in 18 Months; Reevaluate the Use on Citrus After Additional Exposure Data Becomes Available; Cancel Use on Citrus in Arizona and All Other Uses.

Option F is the same as Option E, except that Option F would indicate that the Agency recognizes a different risk/benefit argument for citrus uses between regions. In Arizona, the loss of chlorobenzilate and adoption of alternative miticides is projected to have no economic impact. Cancellation of citrus use in Arizona would yield a marginal reduction in risk to consumers; however, it would eliminate the risk to Arizona applicators.

G. Continue Registration of Chlorobenzilate Use on Citrus, Amend the Terms and Conditions of Registration; Prohibit the Use of Pulp from Chlorobenzilate-Treated Citrus as Cattle Feed; Establish Complementary Tolerances; Cancel All Other Uses.

Option G is the same as Option C, except that Option G would indicate that the Agency is unwilling to accept the potential risk posed to the Florida population through consumption of milk and beef from cattle fed pulp from chlorobenzilate-treated citrus. Accordingly, this option would prohibit the feeding of citrus pulp to cattle and would propose the establishment of complimentary tolerances under the Federal Food, Drug, and Cosmetic Act.

V. Recommended Regulatory Action

OPTION F:

Continue Registration of Chlorobenzilate Use on Citrus in Florida, Texas, and California, Amend the Terms and Conditions of Registration, Require that Identified Exposure Data be Submitted to EPA in 18 Months; Reevaluate the Use on Citrus After Additional ExpoData Becomes Available; Cancel Use on Citrus in Arizona and All Other Uses.

A. Introduction

The foregoing review summarizes and analyzes information on the risks and benefits of the uses of chlorobenzilate and evaluates a series of regulatory options. Several particularly significant factors stand out in the analysis.

With Respect to Risks

- Several studies provide a reliable basis for concluding that chlorobenzilate induces oncogenic effects in mice. Under the Agency's Interim Cancer Assessment Guidelines, these laboratory studies provide substantial evidence that chlorobenzilate poses a cancer risk to man. In view of the human exposure which may result from its uses, chlorobenzilate poses a cancer risk to man of sufficient magnitude to require the Agency to determine whether these uses offer offsetting social, economic, or environmental benefits. The key populations at risk with respect to chlorobenzilate are the U.S. population at large, Florida residents, pesticide applicators, and citrus pickers.

- Chlorobenzilate causes adverse effects to the testes of male rats, and may cause adverse effects to the testes of applicators. Exposure levels of male pesticide applicators are high enough, in comparison to the "no observable effect" levels for adverse testicular effects in rats, to warrant a conclusion that chlorobenzilate may pose a risk of adverse effects to humans of sufficient magnitude to require the Agency to determine whether offsetting social, environmental or economic benefits result from the uses of the pesticide.

With Respect to Benefits

— Chlorobenzilate is used on citrus crops in Florida, Texas, Arizona, and California to control mites. Most use occurs in Florida (72.1%). Significant adverse economic effects, including production losses, would occur if mite pests are not controlled. Chlorobenzilate is utilized in citrus integrated pest management because it is selective to mites and does not kill natural predators and parasites used to control citrus scale pests. Such integrated pest management approaches are used extensively in Florida, and to a lesser extent in the other citrus growing regions. There are several other selective miticides registered for use on citrus crops, and a number of non-selective miticides are also registered for use on these crops.

— Cancellation of chlorobenzilate would significantly increase pest control costs in Florida. Non-selective miticides would be the predominant replacements for chlorobenzilate, for economic and other reasons developed in detail in Section III. This would result in abandoning IPM control of scale, because populations of beneficial insects would be reduced, and large volumes of chemical pesticides would have to be used to control scale insects.

— Relatively small amounts of chlorobenzilate are used in California and only on a few citrus crops in one area. However, cancellation of chlorobenzilate would have significant impacts, because there are no registered alternatives that are regarded as suitable chlorobenzilate replacements.

— The loss of chlorobenzilate and the adoption of alternative miticides is projected to have no net cost to Arizona citrus growers. Using alternatives may disrupt IPM strategies in Arizona, but the extent of any such disruption has not been identified, nor the resulting cost quantified.

— Registered efficacious alternatives are available for each of the other uses of chlorobenzilate; in some cases these alternatives are less expensive and achieve comparable levels of control.

B. Comparison of Options

In selecting a regulatory option, the Agency must decide which of the proposed options achieves the most appropriate balance between risks and benefits. This decision turns in part on the key factual elements summarized above, and in part on the relative merits of each proposed option.

Option A, which would continue registration of all uses, and Option B, which would cancel all uses, represent an all-or-nothing approach to regulation. Under Option A, the Agency would do nothing whatsoever to reduce the known risks of chlorobenzilate nor would it otherwise recognize that the RPAR review confirmed the presumption of oncogenicity. By contrast, Option B would succeed in eliminating risk, but only with substantial increased costs for substitute pesticides and possibly serious environmental and agricultural consequences as the result of disrupting established IPM programs or using unsatisfactory subsitutes. The latter result would be particularly unfortunate because of the Agency's avowed interest in promoting the use of IPM as an alternative to the indiscriminate use of pesticides.

Further, Options A and B are even less tenable in view of the range of available moderately restrictive measures described in Options C through G, which would reduce risk to some extent without significant benefit impacts and would avoid the harsh consequences of across-the-board cancellation. These considerations indicate that Option A would be reasonable only if the benefits clearly outweighed the risks, and if risk reductions could not be achieved without unacceptable benefit consequences. Such considerations further indicate that Option B would be reasonable only if the risks clearly outweigh the benefits, and significant reductions in risks cannot be achieved by measures short of cancellation, without unacceptable benefit impacts. The facts indicate that neither situation pertains, and that these options are not reasonable regulatory measures in this case.

The analysis of risks and benefits of the uses of chlorobenzilate indicates that risks and benefits from citrus uses in Florida, Texas, and California may be close to equilibrium; however, in each situation significant risk reductions can be achieved, without significant impacts on the benefits of the use. With respect to the citrus use in Arizona and the non-citrus uses on the other hand, the analysis suggests that risks exceed benefits, primarily because the projected impacts of cancellation are insignificant while the risks of the uses (particularly to applicators) are not insignificant. Option C and the options which follow it all represent possible regulatory responses to this general assessment of the risks and benefits of chlorobenzilate uses and the balance that should properly be struck between them.

Option C has three distinct components, each of which is designed to reduce the risks of cancer and adverse testicular effects associated with the uses of chlorobenzilate without simultaneously creating the adverse economic, social, or environmental impacts associated with cancellation. In proposing measures to reduce risks by cancelling some uses and restricting the conditions of use for the registrations which remain in effect, this option is distinguishable from Option A which would allow the currently projected risks to continue indefinitely. And by preserving the uses of chlorobenzilate in the major IPM programs, this option is distinguishable from Option B which would eliminate IPM use and produce substantial adverse economic and agricultural impacts.

Options D and G are based on Option C and, like Option C, each would preserve some chlorobenzilate uses under restricted use conditions, thereby reducing risks and also avoiding substantial economic impacts. Each also has a special feature designed to reduce risks which would not be affected by the terms of Option C. The special feature of Option D, cancellation in five years, would reflect a judgment that lifetime exposure to the risks of chlorobenzilate is unacceptable. To ameliorate the adverse economic impact of immediate cancellation as described in Option B, Option D would propose that chlorobenzilate be phased out over a period of five years, during which time satisfactory alternatives may be developed. There is, of course, no certainty that these alternatives would be developed in this time. However, since alternatives are currently under development, cancellation would not be necessary to bring this about.

The special features of Option G, measures to reduce exposure to Florida residents from milk and beef, address the risk which the population in this State may experience. Since these measures would eliminate the market for citrus pulp, this option would reduce growers net income and create a costly disposal problem for processors. To avoid these consequences processors may not purchase chlorobenzilate-treated fruit, and growers may not use chlorobenzilate. In effect, then, elimination of this market could constitute de facto cancellation.

Although Option C and, derivatively, Options D and G would achieve risk reduction without serious adverse economic impacts, these options would not provide measures to validate or expand the information base and thereby make the bases for the proposed regulatory action more certain.

Although the Agency believes that it has made a sound and prudent assessment of the available data, any analysis of this sort requires that a number of uncertainties be dealt with by assumptions drawn from the Agency's experience and expertise. The Agency has strived to use conservative assumptions, consistent with its responsibilities to protect public health. However, it is possible that the Agency has underestimated potential human exposure, and therefore, underestimated the risks of chlorobenzilate use. If so, Option C (which would permit continued use of chlorobenzilate based upon these estimates) would allow a potentially unacceptable risk to continue indefinitely.

Option D presents the reverse problem. If the uncertain data base has resulted in over-estimates of probable human exposure, Option D would propose more stringent regulatory action than would be required to reduce actual risk, and would do so on the speculative assumption that more satisfactory alternatives will be developed.

Options C, D, and E would allow continued use of chlorobenzilate on all citrus with the provisions discussed above. However, there is no information in the record to indicate that substantial benefits derive from the use of chlorobenzilate in Arizona. Acceptance of this option by the Agency would ignore the apparent imbalance of risks and benefits in Arizona, particularly with respect to Arizona applicators.

C. Recommendation of Option F

Option F eliminates the risk from the citrus use in Arizona as well as the risk from all non-citrus uses by cancellation of those uses. This option also reduces the risk to spray applicators, the population at greatest risk from citrus uses of chlorobenzilate, by amending the terms and conditions of registration so that chlorobenzilate may be applied only by certified applicators and only in accord with label directions which reduce exposure.

Specifically, this option requires two amendments to the terms and conditions of chlorobenzilate registrations for citrus use. The first is a requirement that this pesticide be applied only by certified pesticide applicators to ensure, to the extent possible, that pesticides will be applied only by persons skilled and knowledgeable in handling pesticides. The second requirement is that chlorobenzilate be applied only if applicators are protected by protective clothing (hat, gloves, coverall-type suit), respirators, or by working in an enclosed air-filtered cab. The clothing cost would be minimal. The cabs would add a substantial cost to the application process, but if the Agency requires cabs for other pesticides that may be harmful to applicators, this cost would not be fully attributable to the chlorobenzilate regulatory program.

The cancellation and use restriction elements in this option are based on the conclusion that when used in accordance with the modified terms and conditions of registration, the risks associated with the major citrus uses are not unreasonable, in view of the benefits of those uses and the related probable adverse economic impacts of cancellation. In addition, this option also reduces risks appreciably without unacceptable benefit consequences.

Since the continuation of citrus registrations without any other restrictions on use does not reduce the risks to consumers, a decision to continue these uses reflects a determination that these uses do not cause unreasonable adverse effects with respect to this group.

Option F imposes new costs to replace chlorobenzilate with alternatives for non-citrus uses, and other costs in connection with new protection for spray applicators and testing to develop additional data for exposure estimates, but avoids substantial adverse economic effects. Specifically, the cost of cancelling non-citrus uses is minimal compared to the cost of cancelling citrus uses. Further, since cancelling non-citrus uses does not affect IPM programs as would cancelling citrus uses, this option avoids disruption of these programs.

Finally, Option F is preferable to the other proposed options because it provides a regulatory mechanism to clarify and enlarge the data base for the exposure estimates which underlie the risk assessments and risk/benefit analyses. To accomplish this objective, Option F requires chlorobenzilate registrants to develop additional data to confirm or reevaluate the Agency's chlorobenzilate risk assessments and the related regulatory decisions.

REFERENCES

1. Albert, Roy E. (CAG), 1978. EPA memo of June 8, 1978 to J.B. Boyd (SPRD). Comments on the chlorobenzilate risk assessment.
2. Albert, Roy E. (CAG), 1978a. EPA memo of June 23, 1978 to J.B. Boyd (SPRD). Chlorobenzilate risk assessment issues.
3. Albert, Roy E. (CAG), 1978b. Carcinogen Assessment Group's Summary and Conclusions for Assessment of Carcinogenic risk of Chlorobenzilate. Unpublished EPA report dated June 16, 1978.
4. Allen, Jon C., 1978 "The Effect of Citrus Rust Mite Damage on Citrus Fruit Drop", Unpublished report of the University of Florida, IFAS, Agricultural Research and Education Center.
5. Anderson, Elizabeth (CAG), EPA memo of May 29, 1977, to J.B. Boyd (SPRD). CAG assessment of rebuttal points on chlorobenzilate.
6. Barton, Anne (OTS), EPA memo of December 7, 1977, to J.B. Boyd (SPRD). Chlorobenzilate: overall false positive rate.
7. Barton, Anne (OTS), 1977a. EPA memo of February 15, 1977 to J.B. Boyd (SPRD). Statistical analysis of NCI chlorobenzilate study.
8. Boyd, Hudson (CED), 1978. Environmental Fate Profile: Chlorobenzilate. Unpublished report.
9. Boyd, J.B. (SPRD). EPA memo of December 6, 1977 to Edwin L. Johnson (DAA for Pesticide Programs). Chlorobenzilate RPAR Rebuttal Decision.
10. Boyd, J.B. (SPRD). EPA memo of April 1, 1977 to Clayton Bushong (CED). Determination of ecological risks associated with the use of chlorobenzilate alternatives.
11. Boyd, J.B. (SPRD). EPA memo of April 1, 1977 to Lamar Dale (CED). Determination of health risks associated with the use of chlorobenzilate alternatives.
12. Boyd, J.B. (SPRD). EPA memo of March 6, 1978 to SPRD Record. Rebuttals and comments on the chlorobenzilate RPAR.
13. Brogdan, James E., 1976. Extension entomologist, University of Florida, Gainesville, Florida, personal communication of August 6, 1976 to Mark Luttner (cited in Preliminary Benefit Analysis of Chlorobenzilate).
14. Brogdan, James E. and Fred P. Lawrence, 1974. Insects and Mites of Florida Citrus. University of Florida, Institute of Food and Agricultural Sciences, Gainesville, Florida. (cited in Preliminary Benefit Analysis of Chlorobenzilate).

15, Brooke, Donale L., 1973. Citrus production costs and returns in Florida season 1971-1972 with comparisons. Cooperation Extension Service, Institute of Food and Agricultural Sciences. University of Florida.

16. Brooks, R.F., 1977. Integrated Control of Florida Citrus Pests, the Citrus Industry.

17. Brooks, R.F. and J.D. Whitney, 19 . Citrus snow scale control in Florida. Florida Agricultural Experiment Stations Journal, Series No. 4890.

18. Bullock, R.C., 1977. Aerial Application to Florida Citrus (Unpulished Report).

19. Burnam, W.L.. EPA memo of May 4, 1978 to J.B. Boyd (SPRD). Chlorobenzilate Alternatives Review.

20. Burnam, W.L. EPA memo of June 20, 1978 to J.B. Boyd (SPRD). Vendex Review.

21. Bushong, Clayton (CED). EPA memo of August 8, 1977 to J.B. Boyd (SPRD). Chlorobenzilate risk anlaysis, Fish and Wildlife.

22. Cocke, J., G.C. Lyons, and A. Amader, 1978. Texas Citrus Pest Management Proposal. Texas Agricultural Extension Service. The Texas A & M University System.

23. California Dept. of Agriculture, 1972. Pesticide Use Report 1971, Sacramento, California.

24. California Department of Food and Agriculture, 1974 Pesticide Use Report 1973, Sacramento, California. (cited in Preliminary Benefit Analysis.

25. Dale, Lamar (CED). EPA memo of May 4, 1978 to J. B. Boyd (SPRD). Limitation of the chlorobenzilate alternatives review.

26. Dean, H.A., 1975. "Complete biological control of Lepidosaphes beckii on Texas citrus with Aphytis Lepidosaphes." Environ. Entmol. 4:110-114.

27. Dean, H.A., 1955. "Factors affecting biological control of scale insects on Texas citrus." J. Econ. Entmol. 48:444-447.

28. Dean, H.A. and J.C. Bailey, 1964. "Certain post bloom treatments for control of Texas citrus mites and their effect on chaff scale parasites." J. Rio Grande Valley Hort. Soc. 18:29-32.

29. Dean, H.A., W.G. Hart, and S.J. Ingle, 1977. "Pest management considerations of the effects of pesticides on Texas citrus pests and certain parasites." J. Rio Grande Valley Hort. Soc. 31:37-44.

30. Doane Agricultural Service Inc., 1976. "Pesticide Use Data on Selected Specialty Crops," Current Pesticide Use and User Profiles for Selected Pesticide Intensive Crops; Report No. 4, EPA Contract 68-01-1928, St. Louis, Missouri.

31. Edwards, Gordon S. Memo of August 2, 1977 to Elizabeth Anderson (CAG). Comments on criticisms of the Innes study raised by pesticide registrants and within EPA.

32. Federal Register, May 26, 1976. Notice of presumption against registration and continued registraion of pesticide products containing chlorobenzilate. 41(103):21517-21519.

33. Federal Register, June 11, 1976. Notice of presumption against registration and continued registraion of pesticide products containing chlorobenzilate. 41(114):23753.

34. Federal Register, July 14, 1976. Notice of presumption against registration and continued registraion of pesticide products containing chlorobenzilate. 41(136):29015.

35. Federal Register, July 14, 1976. Notice of extension of period for submission of rebuttal evidence and comments with regard to presumption against registration and continued registration of pesticide products containing chlorobenzilate. 41(136):29015.

36. Federal Register, May 25, 1976. Notice on "Interim Procedures and Guidelines for Health Risk and Economic Impact Assessments of Suspected Carcinogens." 41(102):21402-21405.

37. Feldman, R. J. and H. I. Maibach, 1974. "Percutaneous Penetration of Some Pesticides and Herbicides in Man". Tox. Appl. Pharm. 28:126-132.

38. Felkner, I.C., 1978. Commentary on cancer risk from exposure to chlorobenzilate. Unpublished EPA report, dated April 23, 1978.

39. Florida Cooperative Extension Service, 1977. Florida Citrus Spray and Dust Schedule, 1977; Circular 393-C. University of Florida, Gainesville.

40. Food and Drug Administration (FDA), 1971. Food and Drug Administration Advisory Committee on protocols for safety evaluation: Panel on carcinogenesis report on cancer testing in the safety evaluation of food additives and pesticides. Toxicol. Appl. Pharmacol. 20:419-438.

41. Formica, G., W. Blass, and D. Eberle, 1975. "Gas chromatographic residue determination and residues of chlorobenzilate and two major metabolites in plant materials and milk." Meded. Fac. Landbouwwet., Rijks Univ. Gent. 40(2, Pt.2): 1135-1148.

42 French, V., P.J. Rathwell and Reed J. Reeve, 1978. Management of Texas citrus. Citrograph. 63:77-79.

43. Freudenthal, R.I. and P. Leber, 1977. Evaluation of chlorobenzilate toxicology data to determine its potential health hazards to man or domestic animals. Battelle Columbus Laboratories, Columbus, Ohio. (Unpublished).

44. Frith, Charles, 1976. National Center for Toxicological Research. Analysis of Innes Slides and Animal Diagnosis. (Unpublished).

45. Golberg, L., ed., 1974. Carcinogenesis testing of chemicals. CRC Press, Cleveland, Ohio.

46. Griffith, Jack (HEMB). EPA memo of June 20, 1978 to J.B. Boyd (SPRD). Permeability of protective clothing.

47. Gustafson, C.D. and Robert C. Rock, 1977. Lemon Production Costs. Cooperative Extension Service, University of California, San Diego.

48. Huffaker, G., 1978. (Editor). Accomplishments Torward Improving Integrated Pest Management for Citrus. Principles, Strategies, and Tactics of Pest Population Regulation and Control in Major Crop Ecosystems. In press, Wiley and Sons.

49. Hassan, T.K. and C.O. Knowles, 1969. "Behavior of Three C^{14}-labeled Benzilate Acaricides When Applied Topically to Soybean Leaves." J. Econ. Entomal. 62(3):618-619.

50. Horn, H.J., R.B. Bruce, and O.E. Paynter, 1955. Toxicology of chlorobenzilate. J. Agric. Food Chem. 3(9):752-756.

51. Innes, J.R.M., B.M. Ulland, M.G. Valerio, L. Petrucelli, L. Fishbein, E.R. Hart, A.J. Pallotta, R.R. Bates, H.L. Falk, J.J. Gart, M. Klein, I. Mitchell and J. Peters, 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: a preliminary note. J. Nat'l. Cancer Inst. 42:1101-1114.

52. Jeppson, Lee R. (Entomologist), 1976. University of California, Riverside, California, personal communication of September 12, 1976 to Mark Luttner. (cited in Preliminary Benefit Analysis).

53. Knowles, C.O. and S. Ahmad, 1971. "Comparative metabolism of chlorobenzilate, chloropropylate and bromo-propylate. Can. J. Physiol. Pharmacol. 49(6):590-597.

54. Luttner, Mark A., 1978a. EPA memo of April 27, 1978 to J. B. Boyd (SPRD). Estimate of the maximum economic value lost as a result of uncontrolled mite infestations in citrus.

55. Luttner, Mark A., 1978b. EPA memo of June 13, 1978 to J.B. Boyd (SPRD). Vendex as a replacement for chlorobenzilate.

56. Luttner, Mark A., 1978c. EPA memo of June 13, 1978 to J.B.Boyd (SPRD). Vendex.

57. Luttner, Mark A., 1978d. EPA memo of March 31, 1978 to J.B. Boyd (SPRD). Chlorobenzilate exposure analysis.

58. Luttner, Mark A., 1978e. EPA memo of April 14, 1978 to J.B. Boyd (SPRD). Chlorobenzilate: estimated cost of equipment modification requirement.

59. Luttner, Mark A., 1978f. EPA memo of March 28, 1978 to J.B. Boyd (SPRD). Considerations re: restriction of chlorobenzilate use to aerial applications only.

60. Luttner, Mark A., 1978g. EPA memo of May 2, 1978 to J.B. Boyd (SPRD). Chlorobenzilate (Impact of prohibiting use of citrus pulp as cattle feed).

61. Luttner, Mark A., 1977a. Preliminary Benefit Analysis of Chlorobenzilate. Unpublished EPA report.

62. Luttner, Mark A., 1977b. Supplement to the Preliminary Benefit Analysis of Chlorobenzilate. Unpublished EPA report.

63. Maxey, Robert. Pesticides Monitoring Laboratory Memo of June 6, 1978 to Han Tai. Chlorobenzilate.

64. McWhorter, Mike (CED), 1978a. EPA memo of April 5, 1978 to J. B. Boyd (SPRD). Utilization of Dimilin and Hirstuella fungus for control of the citrus mite complex.

65. McWhorter, Mike (CED), 1978b. EPA memo of April 14, 1978, to J. B. Boyd (SPRD). Efficacy of Zardex.

66. Mishra, Lakshmi C. (CED). EPA memo of February 3, 1977 to J.B. Boyd (SPRD). Evaluation of the documents submitted by registrants in rebuttal of chlorobenzilate RPAR.

67. Mishra, L.C., and P. Hebborn, 1971. Ultracentrifugation of mouse plasma containing Rauscher virus. Life Sci. 10 (Part II):1375-1380.

68. Miyazaki, S., G.M. Boush, and F. Matsumura, 1970. "Microbial Degradation of Chlorobenzilate (Ethyl 4,4'-dichlorobenzylate) and chloropropylate (Isopropyl 4,4'-dichlorobenzylate). J. Agric. Food Chem. 18(1):87-91.

69. Murphy, R., R. Kahrs, and A. M. Mattson, 1966. Unpublished Report, Geigy Chemical Corporation.

70. National Cancer Institute (NCI), 1977. Final individual animal pathology table for chlorobenzilate. U.S. Dept. of Health, Eduation, and Welfare, Bethesda, Maryland. (Unpublished).

71. Page, N.P., 1977. Chronic Toxicity and Carcinogenicity Guidelines. J. Envtl. Path. and Tox. 1:161-182.

72. Parrish, Dale W. (HEMB-TSD). Memo of April 6, 1978 to Director, Texas Epidemiologic Studies Program. Assessment of carcinogenesis data (chlorobenzilate).

73. Pertel, Ruth (SPRD). Memo dated January 27, 1978 to J.B. Boyd (SPRD) and Pat Miller (SPRD). Mutagenicity rebuttal on chlorobenzilate: comments.

74. Pertel, Ruth (SPRD). EPA memo of January 31, 1977 to J.B. Boyd (SPRD). Mutagenicity rebuttal on chlorobenzilate: comments.

75. Potrepka, Robert F. (CED), 1978a. EPA memo of June 5, 1978 to J.B. Boyd (SPRD). Testicular atrophy in rats from chlorobenzilate.

76. Potrepka, Robert F. (CED), 1978b. EPA memo of June 9, 1978 to J.B. Boyd (SPRD). Testicular atrophy in rats from chlorobenzilate, addendum to June 5, 1978 memo.

77. Reed, Donald (RD), 1978a. EPA memo of March 17, 1978 to J.B. Boyd (SPRD). Chlorobenzilate residues in milk and meat.

78. Reed, Donald (RD), 1978b. EPA memo of May 3, 1978 to J.B. Boyd (SPRD). Chlorobenzilate residues in milk.

79. Reed, Donald (RD), 1978c. EPA memo of June 2, 1978 to J. B. Boyd (SPRD). EPA Chlorobenzilate residue analysis of citrus pulp.

80 Reed, Donald (RD), 1978d. EPA memo of May 16, 1978 to J.B. Boyd (SPRD). Chlorobenzilate residues in citrus pulp; re: discussion of 5/19/78.

81. Rossi, Lois (SPRD). EPA memo of April 4, 1978 to J. B. Boyd (SPRD). Observed deaths among workers in Chlorobenzilate area of Ciba-Geigy McIntosh plant.

82. Savage, E.P., and R.O. Hayes, 1977. Chlorobenzilate. Colorado State University, Fort Collins, Colorado. (Unpublised).

83. Severn, David J., 1978. Exposure Analysis for Chlorobenzilate. Unpublished EPA report dated March 14, 1978. CONFIDENTIAL.

84. Sontag, J.M., N.P. Page, and U. Saffiotti, 1976. Guidelines for carcinogen bioassay in small rodents. National Cancer Institute, Bethesda, Maryland.

85. Sutton, Harvey J. 1977. Economics of Helicopter Application for Pest Control at Waverley Growers Cooperative (Unpublished Report).

86 Taschenberg, E.F. and John B. Bourke, 1975. "An Air Filter-Pressurization Unit to Protect the Tractor Operator Applying Pesticides," Bull. of Environmental Contamination and Toxicology 13(3):263-268.

87. Technical Services Division (TSD). "Chlorobenzilate Analysis - citrus pulp and feed." Unpublished EPA paper, dated May 22, 1978.

88. Three-Month Feeding Study of Chlorobenzilate, 1965. Bonn, Germany. Submitted to EPA on February 1, 1965 in support of Food Additive Petition No.6H1980.

89. U.S. Dept. of Agriculture (USDA), 1970. PR Notice 70-8. Looseleaf pub.

90. USDA Cooperative State Research Service, USDA/State Chlorobenzilate Assessment Team. An economic and biotic evaluation of chlorobenzilate and its alternatives for rust mite control on citrus in Florida; Recommended chlorobenzilate treatments and evaluation of alternative treatments on citrus in California; the state of chlorobenzilate use in Texas citrus.....1977. 1977, Washington, D.C.

91. USDA, 1977b. Fruit Situation Economic Research Service, U.S. Dept. of Agriculture. TFS-205.

92. USDA Economic Research Service, 1974. Farmers use of pesticides in 1971.... Quantities. Washington, D.C.

93. U.S. Dept. of Health, Education, and Welfare (HEW), 1969. Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health. Washington, D.C.

94. Wilson, 1973. Environment and Birth Defects. Academic Press, New York.

95. Wolfe, H.R., W.F. Durham, and J.F. Armstrong, 1967. "Exposure of Workers to Pesticides." Arch. Environ. Health. 14:622-633. (Cited in Severn, 1978).

96. Woodard Research Corporation, 1966. Chlorobenzilate safety evaluation by dietary feeding to rats for 104 weeks: final report. Geigy Chemical Corporation, Yonkers, New York. (Unpublished). CONFIDENTIAL.

REBUTTAL SUBMISSIONS

1. Alikonis, Robert J., June 25, 1976; Crystal Manufacturing Corporation; [19:30000/3].
2. Alikonis, Robert J., August 27, 1976; Crystal Manufacturing Corporation; [19:30000/3].
3. Alikonis, Robert J., August 24, 1976; Crystal Manufacturing Corporation; [19:30000/3].
4. Alikonis, Robert J., June 25, 1976; Tower Chemical Co.; [11:30000/3].
5. Alikonis, Robert J., August 25, 1976; Tower Chemical Co. [17:30000/3].
6. Alikonis, Robert J., August 27, 1976; Tower Chemical Co.; [23:30000/3A].
7. Alikonis, Robert J., Sept. 9, 1976; Tower Chemical Co.; [33:30000/3].
8. Alikonis, Robert J., June 25, 1976; Trans. Chemical Ind. Inc.; [10:30000/3].
9. Alikonis, Robert J., June 25, 1976; Trans. Chemical Ind. Inc.; [18:30000/3].
10. Alikonis, Robert J., August 27, 1976; Trans. Chemical Ind. Inc.; [25:30000/3C].
11. Altman, Melvin D., June 25, 2976; Shanna; [15:30000/3].
12. Baldi, A., August 11, 1976; Aceto Agricultural Chemicals Corp.; [34:30000/3].
13. Baldi, A., August 26, 1976; Aceto Agricultural Chemicals Corp.; [28:30000/3].
14. Balser, Richard L., Andrew P. Jovanovich, August 27, 1976; Agrico Chemical Co. and Western United Resources, Inc.; [20:30000/3B].
15. Davis, Kent J., DVM, June 7, 1976; [2:30000/3].
16. Goldberg, Melvin, June 10, 1976; Solchem Inc.; [4:30000/3].
17. Goldberg, Melvin, August 26, 1976; Solchem Inc.; [29:30000/3].
18. Griffiths, J.T., June 22, 1976; Florida Citrus Mutual; [8:30000/3].
19. Hall, Graydon B. by Ross A. Pinbauch, June 23, 1976; County of Santa Barbara, CA, Office of Agricultural Commissioner; [13:30000/3].

20. Hinkle, Maureen K., August 27, 1976; Environmental Defense Fund; [21:30000/3].

21. Hunkapiller, Paul, June 25, 1976; Helena Chemical Co.; [9:30000/3].

22. Hunkapiller, Paul, August 27, 1976; Helena Chemical Co.; [26:30000/3].

23. Jeppson, L.R., June 1, 1977; University of California, Riverside Dept. of Entomology; [35:30000/3].

24. Jovanovich, Andrew P., May 17, 1976; Agrico Chemical Co.; [1:30000/3].

25. Jovanovich, Andrew P., August 30, 1976; Agrico Chemical Co.; [31:30000 /3].

26. Jovanovich, Andrew P., October 25, 1976; Western United Resources Inc.; [20A:30000/3].

27. Kendrick, James B. Dr., L.T. Wallace, August 24, 1976; State of California, Dept. of Food & Agriculture; [27:30000/3].

28. Lichty, Ralph W., June 15, 1976; Industry Committee on Citrus Additives & Pesticides, Inc.; [5:30000/3].

29. Lichty, Ralph W., Oct. 5, 1976; Industry Committee on Citrus Additives & Pesticides, Inc.; [5A:30000/3].

30. Little, Kenneth K., June 23, 1976; County of San Diego; [14:30000/3].

31. McCog, Clayton W., Sept. 24, 1976; University of Florida, Institute of Food & Agricultural Sciences; [30:30000/3].

32. McKown, Bobby F., June 18, 1976; Florida Agricultural Research Institute; [7:30000/3].

33. Murphy, R.T., June 7, 1976; Ciba-Geigy; [3:30000/3].

34. Murphy, R.T., Sept. 7, 1976; Ciba-Geigy; [32:30000/3].

35. Murphy, R.T., Nov. 4, 1976; Ciba-Geigy; [22A:30000/3B].

36. Vice, Bob L., June 17, 1976; San Diego County Farm Bureau; [6:30000/3].

37. Weidenfeld, Edward L., June 28, 1976; Attorney for Agrico Co.; [16: 30000/3].

APPENDIX A

SUMMARY OF OTHER CANCER STUDIES

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Horn/Hazelton Study, 1955*

Dose (ppm)	Sex	Number Initial	Number Survived	Complete Necropsy	Rats with Tumors
0	M	20	16	4	2
	F	20	12	10	7
50	M	20	13	5	2
	-	-	-	-	
500	M	20	14	6	2
	F	20	14	6	5

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* Horn, H.J., et al., *J. Agric. Food Chem.*, 3:752-756, 1955.

Woodard Research Corporation
1966 Two-year Rat Study

Dose (ppm)	Sex	Number of Animals Initial	Number of Animals Survived	Number of Animals Necropsied	Animals With Liver Sarcomas
0	M	30	8	5	1
	F	30	11	5	
40	M	30	5	5	
	F	30	14	5	
125	M	30	10	6	4
	F	30	14	5	
400	M	30	10	5	
	F	30	15	5	

SUMMARY* OF RECENTLY COMPLETED NCI BIOASSAY ON FEMALE OSBORNE MENDEL RATS

Dose (ppm)	Site	Tumors	Incidence	Number of Animals
0	Mammary Gland	Fibroadenoma Nos	15	/50
	Pituitary	Chromophobe Adenoma	14	
	Thyriod	C-cell Adenoma	5	
	Uterus Nos	Endometrial Stromal Polyp	4	
	Subcut Tissue/Flank	Hemangiosarcoma	2	
1175	Mammary Gland	Fibroadenoma Nos	14	/48
	Pituitary	Chromophobe Adenoma	11	
	Adrenal	Cortical Adenoma	2	
	Pancreatic Islets	Islet-cell Adenoma	2	
	Thyriod	Follicular-cell Adenoma	2	
2350	Mammary Gland	Fibroadenoma Nos	16	/48
	Pituitary	Chromophobe Adenoma	11	
	Adrenal	Cortical Adenoma	5	
	Uterus Nos	Endometrial Stromal Polyp	4	
	Thyroid	Follicular-cell Carcinoma	3	

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* Provided by NCI, 1977

SUMMARY* OF RECENTLY COMPLETED NCI BIOASSAY ON MALE OSBORNE MENDEL RATS

Dose (ppm)	Site	Tumors	Incidence	Number of Animals
0	Thyroid	Follicular-cell carcinoma	4	/49
	Spleen Nos	Hemangiosarcoma	4	
	Pituitary	Chromophobe Adenoma	4	
	Thyroid	Follicular-cell Adenoma	3	
	Urinary Bladder Nos	Papilloma Nos	3	
1600	Pituitary	Chromophobe Adenoma	7	/50
	Adrenal	Cortical Adenoma	6	
	Multiple Organ Nos	Malig.Lymphoma Histiocyti	2	
	Thyroid	Follicular-cell Adenoma	2	
	Subcut Tissue/Back	Hemangiosarcoma	2	
3200	Pituitary	Chromophobe Adenoma	4	/50
	Thyroid	Follicular-cell Adenoma	4	
	Adrenal	Cortical Adenoma	3	
	Subcut Tissue/Axilla	Fibruma Nos	2	
	Thyroid	Follicular-cell Carcinoma	2	

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* Provided by NCI, 1977

APPENDIX B

OTHER TOXICITY DATA

RODENT SUBACUTE TOXICITY

Rats	44 weeks at 40 ppm	histologic damage to adrenals and pancrease
	44 weeks at 800 ppm	retarded growth; increased hemopoietic activity
	99-day at 2,500 ppm	atrophic testes;
	500 ppm 100 ppm 20 ppm	no effect
	90-day rat feeding study of 2,500 dichlorobnezilate	no effect

Miscellaneous

Sensitivity -

rabbit: eye irritation - severe primary skin irritation - slight to moderate

humans: repeated skin patch test - no primary irritation or sensitization

Neurotoxicity -

Not tested

MUTAGENIC TESTS

Negative in these systems:

- *E. coli*
- *S. typhimurium*
  - Host mediated with *S. typhimurium*
- *Bacillus subtilis*

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FISH ACUTE TOXICITY

Rainbow Trout	48-hour LC_{50}	0.71 mg/l
Sheephead Minnow	48-hour LC_{50}	1.0 mg/l

AVIAN ACUTE TOXICITY

Bobwhite Quail	7-day LC_{50}	3,375 ppm
Mallard Duck	5-day LC_{50}	> 8,000 ppm

RODENT ACUTE TOXICITY

Rats	Oral LD_{50}	702 mg/kg
Mice	Oral LD_{50}	729 mg/kg
Rat	Dermal LD_{50}	> 4 g/kg/day
Rabbit	Dermal LD_{50}	> 10.2 g/kg
Rabbit	Inhalation LC_{50}	> 21; < mg/l air

CHRONIC TOXICITY

Rats	2 years at 50 ppm	Slight decreased size of testes; slight growth effect
	at 500 ppm	Decreased size of testes; retarded growth
Rats	52 weeks at 40 ppm	No effect
	at 125 ppm	Testicular asymetry
	at 400 ppm	Testicular asymetry: markedly reduced Hemoglobin
Rats	2 years at 1,600 ppm	Testicular atrophy
	3,200 ppm	Testicular atrophy
Dogs	2 years; 1 to 14 weeks at 5,000 ppm	Moderate to severe anemia within 14 weeks
	20 to 104 weeks at 3,000 ppm	Organ weight changes; Effects on liver and spleen; Hematopoiesis
	500 ppm	No effect level

APPENDIX C

RISK CONSIDERATIONS RELATING TO PESTICIDE SUBSTITUTES FOR CHLOROBENZILATE

APPENDIX C

RISK CONSIDERATIONS RELATING TO PESTICIDE SUBSTITUTES FOR CHLOROBENZILATE

I. FENBUTATIN-OXIDE

Preliminary inspection of Registration Division file data indicates that toxic effects have been reported for test animals exposed to fenbutatin-oxide in several different studies (Burnam, 1978). Decreased liver, brain, spleen, and kidney weights and decreased body weight gain was reported for animals ingesting 100, 300 and 600 ppm fenbutatin-oxide during the first three months of a two-year chronic feeding study, and for animals ingesting 500 and 1000 ppm during a 28-day subacute study (Shell, Proprietary). Serum alkaline phosphatase was elevated at 300 and 600 ppm, indicating tissue injury at these doses. The no-effect level is 100 ppm for the 3-month exposure and 250 ppm for the subacute exposure (Shell, Proprietary). These changes are indicators of general toxicity.

In the chronic study the testis weights and the testis-to-body-weight ratios were increased at 300 ppm and 600 ppm fenbutatin-oxide, but these changes were not accompanied by hypertrophy or other fenbutatin-oxide related changes. Later in the two-year study, animal growth rates were normal and no fenbutatin-oxide related tumors or lesions were reported.

Adverse reproductive effects were reported in a three-generation reproduction study in rats, with two litters in each generation. The viability index was seriously reduced in the first litter of the first generation at 300 ppm and moderately reduced in both third generation litters at this dose level. At 300 ppm, the parents and pups were smaller in size, were reported to be somewhat hyperactive and irritable at times, and the lactation index was reduced in the second litter. Weaning body weights were reduced in five of the six litters produced during the study. At 100 and 300 ppm, there was a statistically significant decrease ($p = 0.05$) in the testis to body weight ratio, but at 50 ppm the test and control data were comparable. The no-effect level for all parameters including testis weight was 50 ppm (Shell, Proprietary, 1974).

Because fenbutatin-oxide and chlorobenzilate are applied in the same manner, the chlorobenzilate exposure estimates were applied to make the preliminary fenbutatin-oxide risk assessments. Assuming that spray applicators may experience dermal exposure of 0.57 mg/kg and based on a no-effect level of 100 ppm, the margin of safety for subacute exposure to an applicator would be approximately 8.7.[1/]

[1/] The absorption factor for fenbutatin-oxide is unknown and probably less than 10%. If 10% is used, the exposure would be 0.57 mg/kg. Based on a no-effect level of 100 ppm, the margin of safety for subacute exposure to an applicator would be: 100 ppm = 5 mg/kg, then 5 mg/kg divided by 0.57 mg/kg = approximately 8.7.

The margin of safety of 8.7 should be put in perspective. Since exposure is estimated at 0.57 mg/kg/day times 100 = 57 mg/kg, and 1 mg/kg = 20 ppm in the rat's diet. Total dietary exposure is (57 x 20) 1140 ppm. Very few pesticides can be fed at levels of 1140 ppm and those having a no-effect level at 1140 are very, very few in number.

The only conclusion is that any pesticide applied in a manner similar to chlorobenzilate would have a margin of safety or safety factor of considerably less than 100 (Burnham, 1978).

II. DICOFOL

In comparing dicofol with chlorobenzilate the following facts are pertinent: a) both compounds induce hepatocellular carcinomas in male mice; b) chlorobenzilate induces the same kind of lesion in female mice but at a lower rate, and dicofol has no carcinogenic effect on female mice; c) neither compound induces a significant tumorigenic response in maleor female rats; and d) the compounds have similar chemical structure, implying that their mechanism of tumor induction may be the same. In view of these facts, it is legitimate to compare the potency of the compounds. This is done by taking the ratio of the one-hit slope parameters from the NCI experiments. The results are B(dicofol)/B (chlorobenzilate) $= 2.40 \times 10^{-3}/2.02 \times 10^{-4} = 11.9$. Under similar test conditions, dicofol is about 12 times more potent than chlorobenzilate (Albert, 1978b).

III. NON-SELECTIVE SUBSTITUTES

A. Wildlife

Ethion, sulfur, propargite, and carbophenothion do not appear to present significant acute toxicity risks to wildlife from use on citrus (Bushong, 1977).

B. Aquatic Organisms

Acreages involved in citrus uses of chlorobenzilate are large enough to be contiguous with biologically significant bodies of water and the alternatives, ethion and carbophenothion, appear to present more risk from acute effects than chlorobenzilate (fish kills likely to occur in contiguous waters). Propargite appears to present about the same acute risk as chlorobenzilate while sulfur probably presents no acute risk.

C. Human Effects

Use of ethion and carbophenothion present greater risk due to acute toxicity than chlorobenzilate as evidenced by tests of laboratory animals and pesticide episode data (Burnam, 1978). It appears that there would be a greater potential hazard in association with immediate injury to those occupationally involved during or subsequent to use of these substitutes on citrus.

APPENDIX D

LABEL REQUIREMENTS

APPENDIX D

THE FOLLOWING STATEMENTS MUST APPEAR ON THE LABELS OF PESTICIDE PRODUCTS CONTAINING CHLOROBENZILATE

Restricted Use Pesticide

For retail sale to and use only by certified applicators or persons under their direct supervision and only for those uses covered by the certified applicators certification.

General Precautions

A. Take special care to avoid getting chlorobenzilate in eyes, on skin, or on clothing.

B. Avoid breathing vapors or spray mist.

C. In case of contact with skin, wash as soon as possible with soap and plenty of water.

D. If chlorobenzilate gets on clothing, remove contaminated clothing and wash affected parts of body with soap and water. If the extent of contamination is unknown, bathe entire body thoroughly. Change to clean clothing.

E. Wash hands with soap and water each time before eating, drinking, or smoking.

F. At the end of the work day, bathe entire body with soap and plenty of water.

G. Wear clean clothes each day and launder before reusing.

Required Clothing and Equipment for Application

A. Fine weave cotton fabric (Jersey), one-piece jumpsuit, long sleeves, long pants.

B. Wide-brimmed hat.

C. Heavy-duty fabric work gloves.

D. Any article which has become contaminated must be replaced.

E. Face-piece respirator of the type approved for pesticide spray applications by the National Institute for Occupational Safety and Health.

F. Instead of the above specified clothing and equipment, the applicator can use an enclosed tractor cab which provides positive pressure and a filtered air supply. Aerial application may be conducted without the above specified clothing and equipment.

Handling Precautions

A. Heavy-duty rubber or neoprene gloves and apron must be worn during loading, unloading, and equipment clean-up.